WEST Search History

10/079,754

Hide Items | Restore | Clear | Cancel

DATE: Tuesday, January 20, 2004

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR		
☐	L1	histatin$1	147

Displayed KWIC w/o PR.

END OF SEARCH HISTORY

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock NEWS 3 SEP 09 CA/CAplus records now contain indexing from 1907 to the present NEWS 4 DEC 08 INPADOC: Legal Status data reloaded NEWS 5 SEP 29 DISSABS now available on STN NEWS 6 OCT 10 PCTFULL: Two new display fields added NEWS 7 OCT 21 BIOSIS file reloaded and enhanced NEWS 8 OCT 28 BIOSIS file segment of TOXCENTER reloaded and enhanced NEWS 9 NOV 24 MSDS-CCOHS file reloaded NEWS 10 DEC 08 CABA reloaded with left truncation NEWS 11 DEC 08 IMS file names changed NEWS 12 DEC 09 Experimental property data collected by CAS now available in REGISTRY NEWS 13 DEC 09 STN Entry Date available for display in REGISTRY and CA/CAplus NEWS 14 DEC 17 DGENE: Two new display fields added NEWS 15 DEC 18 BIOTECHNO no longer updated NEWS 16 DEC 19 CROPU no longer updated; subscriber discount no longer available NEWS 17 DEC 22 Additional INPI reactions and pre-1907 documents added to CAS databases NEWS 18 DEC 22 IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields NEWS 19 DEC 22 ABI-INFORM now available on STN

NEWS EXPRESS DECEMBER 28 CURRENT WINDOWS VERSION IS V7.00, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003 NEWS HOURS STN Operating Hours Plus Help Desk Availability NEWS INTER General Internet Information NEWS LOGIN Welcome Banner and News Items NEWS PHONE Direct Dial and Telecommunication Network Access to STN NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:23:09 ON 20 JAN 2004

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'CAPLUS' ENTERED AT 12:23:22 ON 20 JAN 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1907 - 20 Jan 2004 VOL 140 ISS 4
FILE LAST UPDATED: 19 Jan 2004 (20040119/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s histatin#/bi,ab 222 HISTATIN#/BI 188 HISTATIN#/AB
L1 222 HISTATIN#/BI,AB

=> s l1 not 2004/py 47945 2004/PY
L2 218 L1 NOT 2004/PY

=> s l2 not 2003/py 1069500 2003/PY

L3 181 L2 NOT 2003/PY

=> d l3 1-181 bib ab

L3 ANSWER 1 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:68107 CAPLUS
DN 138:131054
TI Safety and clinical effects of topical ***histatin*** gels in humans with experimental gingivitis
AU Paquette, D. W.; Simpson, D. M.; Friden, P.; Braman, V.; Williams, R. C.
CS Department of Periodontology, Comprehensive Center for Inflammatory Disorders, School of Dentistry, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
SO Journal of Clinical Periodontology (2002), 29(12), 1051-1058
CODEN: JCPEDZ; ISSN: 0303-6979
PB Blackwell Munksgaard
DT Journal
LA English
AB Background: Our research group has recently reported that exogenously applied ***histatins*** can inhibit plaque accumulation and gingival inflammation in a preclin. canine model (Paquette et al. 1997). Objectives: The aims of the present double-blinded, randomized, controlled clin. trial were to evaluate the safety and toxicity of three ***histatin*** (P-113) concns. in gel formulations, and to assess potential clin. benefit on the development of gingivitis (partial mouth design). Material and methods: One hundred and six healthy subjects were recruited and brought to optimal gingival health (GI < 0.5) prior to treatment initiation. At baseline, eligible subjects were randomized for one of the following treatments: (1) placebo; (2) 0.0625% P-113; (3) 0.125% P-113; and (4) 0.375% P-113. Patients self-applied gels twice daily for 29 days to the maxillary right quadrant with the use of customized stents. In addn., patients deferred all oral hygiene procedures within this quadrant for the duration of the treatment period. Safety was assessed in terms of phys. and oral examns., clin. lab. testing and recording of adverse events. Clin. indexes were measured weekly and included gingival index (GI), plaque index (PI) and %BOP. Results: All study formulations were well tolerated by patients, and no differences in adverse event occurrences were noted among treatment groups, including taste alteration or staining. For the intent-to-treat population, significantly smaller %BOP changes were noted in subjects treated with 0.0625, 0.125 and 0.375% P-113 gels (17.4, 18.18 and 17.9%, resp.) vs. placebo (28.0%) ($p < 0.05$) at day 29. When groups were compared in terms of per cent responders (change in %BOP < 15 or < 20%), P-113 treatment groups exhibited a higher frequency of

response, esp. for the 0.0625 and 0.125% P-113 formulations ($p < 0.05$). Although no statistically significant intergroup differences were noted for changes in GI or PI among all subjects (intent-to-treat population), significantly smaller changes in PI at day 22 were obsd. among compliant individuals (defined as subjects using >60% of the target gel mass) administering P-113 gels as compared with compliant placebo subjects ($p < 0.05$). Conclusions: These data indicate safety and tolerance of P-113 gels for topical oral use in human subjects. These data also suggest that P-113 gels administered twice daily may reduce exptl. gingivitis as measured with bleeding on probing in humans.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:944123 CAPLUS
DN 138:150138
TI Susceptibility of Candida albicans isolates from the oral cavities of HIV-positive patients to ***histatin*** -5
AU Nikawa, Hiroki; Jin, Chen; Makihira, Seicho; Hamada, Taizo; Samaranayake, Lakshman P.
CS Faculty of Dentistry, Hiroshima University, Hiroshima, Japan
SO Journal of Prosthetic Dentistry (2002), 88(3), 263-267
CODEN: JPDEAT; ISSN: 0022-3913
PB Mosby, Inc.
DT Journal
LA English
AB Oral surfaces, including the denture-fitting surface, may serve as a reservoir for disseminated candidal infections, particularly in immunocompromised hosts such as patients with AIDS. ***Histatins*** are a group of small, cationic antifungal peptides present in human saliva. There is limited information on the antifungal activity of peptides against Candida albicans isolates from HIV-pos. patients. This study investigated the fungicidal effects of ***histatin*** -5 against oral isolates of C. albicans from HIV-pos. and HIV-neg. patients. An isolate of C. albicans from each of 2 HIV-pos. patients (both male) and 3 HIV-neg. patients (2 male and 1 female) was obtained. American Type Culture Collection 90028 served as a ref. strain. All isolates were identified with sugar assimilation tests and the germ tube test. Fungicidal assays were performed on exponential C. albicans cells in the presence or absence of 0.315 to 50 .mu.m of ***histatin*** -5. Numerical data were subjected to 1-way anal. of variance and Tukey's multiple range test ($P<.05$). ***Histatin*** -5 (50 .mu.m) killed more than 95% of C. albicans isolates from HIV-neg. patients and more than 90% of isolates from the ref. strain. The same treatment induced 75.3% and 66.1% loss of viability in C. albicans isolates taken from HIV-pos. patients (A1 and A2 cells, resp.). The difference between the fungicidal effects in the HIV-pos. and HIV-neg. groups was significant ($P<.05$). Within the limited population of this study, C. albicans isolates from the oral cavities of HIV-pos. patients were less sensitive to ***histatin*** -5 than oral isolates from HIV-neg. patients.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:871997 CAPLUS
DN 139:143385
TI Effects of carbohydrate polymers applicable in saliva substitutes on the anti-Candida activity of a ***histatin*** -derived peptide
AU Ruissen, Anita L. A.; Groenink, Jasper; Lommerse, Cock H.; Van't Hof, Wim.; Veerman, Enno C. I.; Nieuw Amerongen, Arie V.
CS Department of Dental Basic Sciences, Section of Oral Biochemistry, Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam, 1081 BT, Neth.
SO Archives of Oral Biology (2002), 47(11), 749-756 CODEN: AOBIAR; ISSN: 0003-9969
PB Elsevier Science Ltd.
DT Journal
LA English
AB The effects of polymers applicable in saliva substitutes on the anti-Candida activity of the cationic antimicrobial peptide dhvar1 were investigated. Dhvar1 is a deriv. of the 14 C-terminal amino acids of ***histatin*** 5. The effects of the following polymers were tested: uncharged hydroxyethylcellulose (HEC), neg. charged xanthan (XG) and three types of neg. charged CM-cellulose (CMC) of identical mass but different degrees of carboxylic acid-group substitution (DS). The effects were tested at pH 4.0, 7.0 and 8.5 in a killing assay. HEC had no effect at any pH tested; XG and the three types of CMC caused a decrease in activity at increasing concns. Within the CMC group, inhibition increased slightly with increasing DS. These results suggest that the redn. in activity assocd. with these polymers is the result of electrostatic interaction between the pos. charged peptides and the neg. charged polymers. In the absence of polymers, no effect of pH was found on the activity of dhvar1. In the presence of the charged polymers XG and CMC, lowering the pH from 7.0 to 4.0 resulted in a decrease of dhvar1 activity. It was concluded that, with respect to the retention of activity, HEC is the most appropriate polymer for use in combination with dhvar1. However, for use in saliva substitutes XG seems more suitable because of its rheol. properties. If XG or CMC are to be used, their reductive effect on the anti-Candida activity of dhvar1 should be compensated for by increasing the peptide dose.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:726605 CAPLUS
DN 138:35870
TI Characterization of the mitochondrial respiratory pathways in Candida albicans
AU Helmerhorst, Eva J.; Murphy, Michael P.; Troxler, Robert F.; Oppenheim, Frank G.
CS Goldman School of Dental Medicine, Boston University, Boston, MA, 02118, USA
SO Biochimica et Biophysica Acta (2002), 1556(1), 73-80 CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal
LA English
AB C. albicans is an opportunistic oral pathogen. The flexibility of this microorganism in response to environmental changes includes the expression of a CN--resistant alternative respiratory pathway. In the present study, we characterized both conventional and alternative respiratory pathways and detd. their ADP/O ratios, inhibitor sensitivity profiles, and the impact of the utilization of either pathway on susceptibility to commonly used antimycotics. O2 consumption by isolated mitochondria using NADH or malate/pyruvate as respiratory substrates indicated that C. albicans cells express both cytoplasmic and matrix NADH-ubiquinone oxidoreductase activities. The ADP/O ratio was higher for malate/pyruvate (2.2 .+-. 0.1), which generate NADH in the matrix, than for externally added NADH (1.4 .+-. 0.2). In addn., malate/pyruvate respiration was rotenone-sensitive, and an enzyme activity assay further confirmed that C. albicans cells express Complex I activity. Cells grown in the presence of antimycin A expressed the CN--insensitive respiratory pathway. Detn. of the respiratory control ratio (RCR) and ADP/O ratios of

mitochondria from these cells indicated that electron transport from ubiquinone to O2 via the alternative respiratory pathway was not coupled to ATP prodn.; however, an ADP/O ratio of 0.8 was found for substrates that donate electrons at Complex I. Comparison of antifungal susceptibility of C. albicans cells respiring via the conventional or alternative respiratory pathways showed that respiration via the alternative pathway does not reduce the susceptibility of cells to a series of clin. employed antimycotics (using Fungitest), or to the naturally occurring human salivary antifungal peptide, ***histatin*** 5.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:669374 CAPLUS
DN 138:22462
TI Comparison of Inhibitory Activity on Calcium Phosphate Precipitation of Acidic Proline-Rich Proteins, Statherin, and ***Histatin*** -1
AU Tamaki, N.; Tada, T.; Morita, M.; Watanabe, T.
CS Graduate School of Medicine and Dentistry, Department of Oral Health, Okayama University, Okayama, 700-8525, Japan
SO Calcified Tissue International (2002), 71(1), 59-62 CODEN: CTINDZ; ISSN: 0171-967X
PB Springer-Verlag New York Inc.
DT Journal
LA English
AB This study quant. compares the inhibition of calcium phosphate (CaP) pptn. by the salivary acidic proline-rich proteins (PRPs) statherin and ***histatin*** -1. Saliva and CaCl2 in 125 mM imidazole buffer (pH 7.0) were incubated with potassium phosphate and a hydroxyapatite (HAP) suspension, for 30 min at 25.degree.C, then filtered through nitrocellulose. The calcium concn. in the filtrate was measured by at. absorption spectrophotometry, then deducted from that in the initial soln. to det. the amt. of CaP pptn. after 30 min. The values of the inhibition of CaP pptn. relative to crude parotid saliva were 4.7, 4.9, 6.9, and 65.8 for ***histatin*** -1, large PRPs, small PRPs, and statherin, resp.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:639172 CAPLUS
DN 137:307249
TI Human salivary ***histatin*** 5 causes disordered volume regulation and cell cycle arrest in Candida albicans
AU Baev, Didi; Li, Xuewei S.; Dong, Jin; Keng, Peter; Edgerton, Mira
CS Department of Oral Biology, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Infection and Immunity (2002), 70(9), 4777-4784 CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
AB Human salivary ***histatin*** 5 (Hst 5) is a nonimmune salivary protein with antifungal activity against an important human pathogen, Candida albicans. The candidacidal activity of ***histatins*** appears to be a distinctive multistep mechanism involving depletion of the C. albicans intracellular ATP content as a result of nonlytic ATP efflux. Hst 5 caused a loss of cell viability concomitant with a decrease in cellular vol. as detd. both by a classical candidacidal assay with exogenous Hst 5 and by using a genetically engineered C. albicans strain expressing Hst 5. Preincubation of C. albicans cells with pharmacol. inhibitors of anion transport provided complete or substantial protection from Hst 5-induced killing and vol. redn. of cells. Moreover, intracellular expression of Hst 5 resulted in a redn. in the population mean cell vol. that was accompanied by an increase in the percentage of unbudded cells and C. albicans cells in the G1 phase. Following expression of Hst 5, the smallest cells sorted by fluorescence-activated cell sorting from the total population did not replicate and were exclusively in the G1 phase. Cells with intracellularly expressed Hst 5 had greatly reduced G1 cyclin transcript levels, indicating that they arrested in the G1 phase before the onset of Start. Our data demonstrate that a key determinant in the mechanism of Hst 5 toxicity in C. albicans cells is the disruption of regulatory circuits for cell vol. homeostasis that is closely coupled with loss of intracellular ATP. This novel process of fungicidal activity by a human salivary protein has highlighted potential interactions of Hst 5 with vol. regulatory mechanisms and the process of yeast cell cycle control.
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:636010 CAPLUS
DN 137:261541
TI ***Histatin*** 5 and derivatives. Their localization and effects on the ultra-structural level
AU Ruissen, A. L. A.; Groenink, J.; Van 't Hof, W.; Walgreen-Weterings, E.; van Marle, J.; van Veen, H. A.; Voorhout, W. F.; Veerman, E. C. I.; Nieuw Amerongen, A. V.
CS Academic Centre for Dentistry Amsterdam, Department of Dental Basic Sciences, Vrije Universiteit, Amsterdam, 1081 BT, Neth.
SO Peptides (New York, NY, United States) (2002), 23(8), 1391-1399 CODEN: PPTDD5; ISSN: 0196-9781
PB Elsevier Science Inc.
DT Journal
LA English
AB ***Histatins*** , a family of cationic peptides present in saliva, are active against the opportunistic yeast Candida albicans. The mechanism of action is still unclear. ***Histatin*** 5 and more potent synthetic variants, dhvar4 and dhvar5, were used to study localization and effects on morphol. on the ultra-structural level. Although all peptides induced leakage, no assocn. with the plasma membrane, indicative for permanent pores, was obsd. with immuno-gold-labeling. Freeze-fracturing showed severe changes of the plasma membrane. Together with, for the dhvars, the loss of intracellular integrity, this suggests that leakage may be a secondary effect rather than an effect of formation of permanent pores.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:619202 CAPLUS
DN 138:12894
TI Effect of ***histatin*** 5, a specific protease inhibitor, on cytotoxic activity of porphyromonas gingivalis protease in cultured human gingival fibroblasts
AU Wang, Pao-Li; Kanehira, Takashi; Oido, Mari; Fujii, Takeo; Kowashi, Yusuke; Ohura, Kiyoshi; Kuboki, Yoshinori
CS Department of Pharmacology, Osaka Dental University, Osaka, 573-1121, Japan
SO Journal of Hard Tissue Biology (2002), 11(1), 16-19 CODEN: JHTBFF; ISSN: 1341-7649
PB Society of Hard Tissue Biology
DT Journal
LA English
AB We examd. the effects of ***histatin*** 5 on an arginine-specific cysteine protease obtained from Porphyromonas

gingivalis (Arg-gingipain; P.g. protease) in cultured human gingival fibroblasts (HGFs). Cultures of HGFs were incubated for 12 h with P.g.protease and/or ***histatin*** 5. In the HGF culture incubated with P.g. protease alone, morphol. examn. revealed detachment of HGFs from the dish, and MTT assay showed a decrease in cell no. We found that P.g. protease destroyed the HGFs. However, HGF culture incubated with both ***histatin*** 5 and P.g. protease showed no morphol. changes and no decrease in cell no. Thus ***histatin*** 5 prevented the protease-induced inhibition of the HGF growth.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:537710 CAPLUS
DN 137:103302
TI ***Histatin*** -derived peptides: potential agents to treat localized infections
AU Rothstein, David M.; Helmerhorst, Eva J.; Spacciapoli, Peter; Oppenheim, Frank G.; Friden, Phillip
CS Demegen, Inc., Watertown, MA, 02472, USA
SO Expert Opinion on Emerging Drugs (2002), 7(1), 47-59
CODEN: EOEDA3
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
AB A review. ***Histatins*** are a family of histidine-rich, cationic peptides composed of up to 38 amino acids. They are secreted by the salivary glands of humans and some subhuman primates and are thought to be part of the host defense system in the oral cavity. ***Histatins*** exhibit in vitro activity against both bacteria and yeast, common to other antimicrobial peptides. Because of these activities, ***histatin*** -based peptides could play an important role in the treatment and prevention of infectious diseases. A 12 amino acid amidated fragment of ***histatin*** 5, designated P-113, has been identified as the smallest fragment that retains antimicrobial activity comparable to the parent compd. Animal studies and human clin. trials showed that P-113 has potential in preventing the development of gingivitis, with no adverse side effects. ***Histatin*** peptides also could be used for other therapeutic applications in which the infection is localized and accessible via topical delivery, such as treatment of candidiasis (thrush) and mucositis in the oral cavity, skin infections and treatment of lung infections afflicting cystic fibrosis patients.
RE.CNT 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:531094 CAPLUS
DN 137:74695
TI Inhibitory effect of synthetic ***histatin*** 5 on leukotoxin from Actinobacillus actinomycetemcomitans
AU Murakami, Y.; Xu, T.; Helmerhorst, E. J.; Ori, G.; Troxler, R. F.; Lally, E. T.; Oppenheim, F. G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118, USA
SO Oral Microbiology and Immunology (2002), 17(3), 143-149
CODEN: OMIMEE; ISSN: 0902-0055
PB Blackwell Munksgaard
DT Journal
LA English
AB Actinobacillus actinomycetemcomitans is a gram-neg. bacterium strongly implicated in the pathogenesis of juvenile periodontitis. This periodontal pathogen synthesizes a leukotoxin that destroys human polymorphonuclear leukocytes (PMNs), and this toxin is thought to be responsible for the virulence of A. actinomycetemcomitans. It was therefore of interest to assess whether major virulence factors of periodontal pathogens were neutralized by salivary components. This study focuses on the effect of ***histatins*** , components of the nonimmune oral defense system, on leukotoxin activity. Leukotoxin was extd. with polymyxin B from freshly grown anaerobic cultures of A. actinomycetemcomitans strain Y4. PMNs isolated from blood of healthy human volunteers were incubated in a cytotoxicity assay contg. PMNs (107 cells/mL) and leukotoxin prepn. (0-500 .mu.g/mL) in Hanks' balanced salt soln. at 37.degree. for 0-120min with or without synthetic ***histatin*** 5 (0-500 .mu.M). Cytotoxicity was measured by release of lactate dehydrogenase (LDH) at different time intervals. ***Histatin*** 5 neutralized the toxic effect of the leukotoxin prepn. in a concn.-dependent manner, with an IC50 value of 150 .mu.M. When PMNs were preincubated with ***histatin*** 5 (300 .mu.M), washed and subsequently exposed to leukotoxin, no protective effect was obsd. This observation suggests a mechanism of inhibition whereby ***histatin*** 5 either directly neutralizes the leukotoxin or interferes with the leukotoxin-PMN interaction. The inhibitory effect of ***histatin*** 5 on leukotoxic activity may suggest a new biol. function of ***histatins*** in the oral cavity as a naturally occurring secondary antibiotic.
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:517663 CAPLUS
DN 137:90066
TI Purification of kinase activity from primate parotid glands
AU Lamkin, M. S.; Lindhe, P.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118, USA
SO Journal of Dental Research (2001), 80(10), 1890-1894
CODEN: JDREAF; ISSN: 0022-0345
PB International Association for Dental Research
DT Journal
LA English
AB Salivary secretions contain phosphoproteins that contain phosphorylation sites composed of Ser residues in acidic environments. The hypothesis of this study is that a protein kinase responsible for phosphorylating these proteins is similar to kinases that phosphorylate proteins in other glandular secretions. Here, homogenates and subfractions from macaque (Macaca fascicularis) parotid glands were found to be able to phosphorylate synthetic peptide substrates contg. each of the phosphorylation sites in the acidic proline-rich proteins, statherin, and ***histatin*** 1. Enzyme activity was purified from Golgi membranes to >220-fold by extn. with Triton X-100 and affinity chromatog. with the use of immobilized ATP. The enzyme preferred substrates contg. Ser residues in a specific acidic environment, particularly those contg. the Ser-Xaa-acidic sequence, preferred ATP over GTP, and was sensitive to high concns. of heparin. These characteristics were similar to those reported for Golgi app. casein kinase, which phosphorylates casein in vivo. Based on these observations, the parotid gland kinase may be related to other Golgi-localized protein serine kinases.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:512420 CAPLUS
DN 137:332737

TI Conformation of the peptide antibiotic - ***histatin*** 8 in aqueous and non aqueous media
AU Tauro, Savita; Coutinho, Evans; Srivastava, Sudha
CS Department of Pharmaceutical Chemistry, Bombay College of Pharmacy, Mumbai, 400 098, India
SO Letters in Peptide Science (2001), 8(6), 295-307 CODEN: LPSCEM; ISSN: 0929-5666
PB Kluwer Academic Publishers
DT Journal
LA English
AB ***Histatin*** 8 (Lys1-Phe-His-Glu-Lys5-His-His-Ser-His-Arg10-Gly- Tyr12) belongs to a group of related neutral and basic histidine rich peptides present in human salivary secretions that possess fungicidal and bactericidal activities. The conformation of this peptide has been examd. by 1H and 13C 2D-NMR in DMSO-d6, water (pH 4.0) and 40% HFA solns. MD simulations incorporating NMR data was used to generate the soln. conformations. The structures were refined by MARDIGRAS employing the RANDMARDI approach. In both DMSO-d6 and water, the peptide is seen to adopt a .beta.-pleated sheet, while HFA induces an .alpha.-helix structure. The role of these structures in its mechanism of action has been explained.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:465423 CAPLUS
DN 137:228256
TI Human secretory signal peptide description by hidden Markov model and generation of a strong artificial signal peptide for secreted protein expression
AU Barash, Steve; Wang, Wei; Shi, Yanggu
CS Department of Information Technology, Human Genome Sciences, Inc., Rockville, MD, 20850, USA
SO Biochemical and Biophysical Research Communications (2002), 294(4), 835-842 CODEN: BBRCA9; ISSN: 0006-291X
PB Elsevier Science
DT Journal
LA English
AB A hidden Markov model (HMM) has been used to describe, predict, identify, and generate secretory signal peptide sequences. The relative strengths of artificial secretory signals emitted from the human signal peptide HMM (SP-HMM) correlate with their HMM bit scores as detd. by their effectiveness to direct alk. phosphatase secretion. The nature of the signal strength is in effect the closeness to the consensus. The HMM bit score of 8 is exptl. detd. to be the threshold for discriminating signal sequences from non-secretory ones. An artificial SP-HMM generated signal sequence of the max. model bit score (HMM +38) was selected as an ideal human signal sequence. This signal peptide (secrecon) directs strong protein secretion and expression. We further ranked the signal strengths of the signal peptides of the known human secretory proteins by SP-HMM bit scores. The applications of high-bit scoring HMM signals in recombinant protein prodn. and protein engineering are discussed.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:395348 CAPLUS
DN 137:60882
TI Circadian rhythms of ***histatin*** 1, ***histatin*** 3, ***histatin*** 5, statherin and uric acid in whole human saliva secretion
AU Castagnola, M.; Cabras, T.; Denotti, G.; Fadda, M. B.; Gambarini, G.; Lupi, A.; Manca, I.; Onnis, G.; Piras, V.; Soro, V.; Tambaro, S.; Messana, I.
CS Inst. of Biochemistry and Clinical Biochem., Fac. of Medicine, Catholic Univ., Rome, Italy
SO Biological Rhythm Research (2002), 33(2), 213-222 CODEN: BRHREI; ISSN: 0929-1016
PB Swets & Zeitlinger B.V.
DT Journal
LA English
AB The circadian rhythms of ***histatins*** 1, 3, 5, statherin, and uric acid were investigated in whole human saliva. The ***histatins*** showed a rhythm approx. synchronous with salivary flow rate (acrophase, .apprx.5 pm), the higher amplitude pertaining to ***histatin*** 1 (.apprx.50% of the mesor). Uric acid showed a large rhythm asynchronous with flow rate and ***histatin*** concns. (4.4 .+-. 1.4 am). Statherin did not show a significant circadian rhythm on 5 of 6 volunteers. This finding confirms that the secretion route of statherin is different from that of ***histatins*** .
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:256856 CAPLUS
DN 137:2958
TI Structure-based design of potent ***histatin*** analogues
AU Brewer, Dyanne; Lajoie, Gilles
CS Department of Chemistry, Guelph-Waterloo Centre for Graduate Work in Chemistry and Biochemistry, University of Waterloo, Waterloo, ON, N2L 3G1, Can.
SO Biochemistry (2002), 41(17), 5526-5536 CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB Conformational studies of human salivary peptide, ***histatin*** 3 (Hst3), were performed by NMR and CD spectroscopy in a membrane-mimicking environment. The structural information that was obtained was used in the design of peptide analogs with improved antifungal activity. In the presence of increasing concns. of L-.alpha.-dimyristoylphosphatidylcholine (L-.alpha.-DMPC) lipid vesicles, a dramatic increase in a min. at 198 nm is obsd. in the CD spectra of Hst3. The NMR data of Hst3 in the presence of L-.alpha.-DMPC lipid vesicles reveal the proximity of residues Y10 and S20, indicating the existence of a more compact structure. Peptide analogs were designed on the basis of this observation, which incorporated a disulfide bond to stabilize an extended loop in this region of the sequence. One of these, peptide 4, was 100 times more potent than Hst5 against Saccharomyces cerevisiae cells. Conformational anal. of peptide 4 revealed a looped structure with charged residues protruding on the outside surface, while a combination of arom. residues and histidines are packed into an internal core.
RE.CNT 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:200145 CAPLUS
DN 137:210438
TI Clinical and microbial evaluation of a ***histatin*** -containing mouthrinse in humans with experimental gingivitis: A phase-2 multi-center study
AU Van Dyke, Thomas; Paquette, David; Grossi, Sara; Braman, Virginia; Massaro, Joseph; D'Agostino, Ralph; Dibart, Serge; Friden, Phillip

CS Boston University Goldman School of Dental Medicine, Boston, MA, USA
SO Journal of Clinical Periodontology (2002), 29(2), 168-176 CODEN: JCPEDZ; ISSN: 0303-6979
PB Blackwell Munksgaard
DT Journal
LA English
AB P-113, a 12 amino acid ***histatin*** -based peptide, was evaluated in a mouthrinse formulation for safety and efficacy in a phase 2 multi-center clin. study. Two hundred ninety-four healthy subjects abstained from oral hygiene procedures and self-administered either 0.01% P-113, 0.03% P-113 or placebo mouthrinse formulations twice daily over a 4-wk treatment period. During this time, the safety, anti-gingivitis, and anti-plaque effects of P-113 were evaluated. There was a significant redn. in the change from baseline to Day 22 in bleeding on probing in the 0.01% P-113 treatment group of the intent to treat population (p=0.049). Non-significant trends in the redn. of the other parameters were obsd. in this population (p.gtoreq.0.159). A sub-group of subjects which developed significant levels of disease within the four-week timeframe of the study was identified based on baseline gingival index scores .gtoreq.0.75. Significant findings were obsd. for bleeding on probing, gingival index and plaque index within this population ($p<0.05$). There were no treatment-related adverse events, and there were no adverse shifts in supragingival microflora during the study. Significant amts. of the peptide were retained in the oral cavity following rinsing. These data suggest that P-113 mouthrinse is safe and reduces the development of gingival bleeding, gingivitis and plaque in the human exptl. gingivitis model.
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:182951 CAPLUS
DN 137:90
TI Antimicrobial peptides: therapeutic potential for the treatment of Candida infections
AU Lupetti, Antonella; Danesi, Romano; Van 't Wout, Jan W.; Van Dissel, Jaap T.; Senesi, Sonia; Nibbering, Peter H.
CS Department of Infectious Diseases, Leiden University Medical Center (LUMC), Leiden, Neth.
SO Expert Opinion on Investigational Drugs (2002), 11(2), 309-318 CODEN: EOIDER; ISSN: 1354-3784
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
AB A review. The increasing frequency of fungal infections in immunocompromised patients together with the emergence of strains resistant to currently used antifungal drugs point to an increased need for a new class of antimycotics. Antimicrobial peptides are promising candidates for the treatment of fungal infections since they have both mechanisms of action distinct from available antifungal agents and the ability to regulate the host immune defense systems as well. This review focuses on Candida albicans as a large amt. of work on the mechanisms of action of classical antifungals as well as antimicrobial peptides, such as defensins, protegrins, ***histatins*** , and lactoferrin (LF)-derived peptides, was performed in this yeast. Analogs of these antimicrobial peptides and combinations of antimicrobial peptides with classical antimycotics are under investigation for treatment of candidiasis.
RE.CNT 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:77402 CAPLUS
DN 136:139651
TI Dentifrices containing protein adsorption inhibitors and disinfectants
IN Shimotoru, Rei; Okajima, Miyuki; Kobayashi, Hisataka; Tokimitsu, Ichiro
PA Kao Corp., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI JP 2002029948 A2 20020129 JP 2000-211546 20000712
PRAI JP 2000-211546 20000712
AB Dentifrices for the prevention of stains and plaques on the surface of teeth comprise (1) protein adsorption inhibitors such as statherin, ***histatin*** , and phosphated polysaccharides and (2) bactericides. Fractions contg. statherin and ***histatin*** were isolated from saliva and in vitro tested for inhibiting activities of glycoprotein adsorption onto apatite plates.

L3 ANSWER 19 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:933702 CAPLUS
DN 136:380853
TI Genetically engineered human salivary ***histatin*** genes are functional in Candida albicans: development of a new system for studying ***histatin*** candidacidal activity
AU Baev, Didi; Li, Xuewei; Edgerton, Mira
CS Departments of Oral Biology, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Microbiology (Reading, United Kingdom) (2001), 147(12), 3323-3334 CODEN: MROBEO; ISSN: 1350-0872
PB Society for General Microbiology
DT Journal
LA English
AB ***Histatins*** are a structurally related family of salivary proteins known as histidine-rich proteins that are produced and secreted by the human major salivary glands. In vitro, ***histatins*** are potent cytotoxic proteins with selectivity for pathogenic yeasts including Candida albicans. Studies that investigate the mechanism of action of ***histatin*** proteins upon this important human pathogen have used a candidacidal assay in which the ***histatin*** is applied extracellularly. In order to develop a model system to study the mechanism of ***histatin*** action independently from binding and translocation events, the authors constructed C. albicans strains that contain chromosomally encoded human salivary ***histatin*** genes under the control of a regulated promoter. Intracellular expression of either ***histatin*** 5 or ***histatin*** 3 induced cell killing and ATP release in parallel. Since ***histatin*** killing can be initiated solely from intracellular sites, extracellular binding and internalization are preceding transport events. Thus the mechanism of ***histatin*** -induced ATP release does not require extracellular binding, and intracellular targets alone can activate ATP release. By employing a codon-optimization strategy it was shown that expression of heterologous sequences in C. albicans can be a useful tool for functional studies.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:932396 CAPLUS
DN 136:197365
TI Nonmucin proteins of saliva with high homology of polypeptide chains

AU Zalewska, Anna; Pietruska, Malgorzata Dorota; Knas, Malgorzata; Zwierz, Krzysztof
CS Zakl. Biochem. Farm., Akad. Med., Bialystok, 15-222, Pol.
SO Postepy Higieny i Medycyny Doswiadczalnej (2001), 55(5), 733-754 CODEN: PHMDAD; ISSN: 0032-5449
PB Wydawnictwo Continuo
DT Journal; General Review
LA Polish
AB A review. To nonmucin proteins of human saliva belong: cystatins, statherin, ***histatins*** and acidic proline-rich protein. These saliva proteins influence hard and soft tissues by forming a pellicle layer on oral mucosa and enamel, by taking part in removing bacteria or initiating of bacterial colonization. Most of them are able to inhibit the formation of dental calculus and control the calcium phosphate homeostasis.

L3 ANSWER 21 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:929611 CAPLUS
DN 136:115329
TI Killing of Candida albicans by ***histatin*** 5: cellular uptake and energy requirement
AU Gyurko, Csilla; Lendenmann, Urs; Helmerhorst, Eva J.; Troxler, Robert F.; Oppenheim, Frank G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118-2392, USA
SO Antonie van Leeuwenhoek (2001), 79(3-4), 297-309 CODEN: ALJMAO; ISSN: 0003-6072
PB Kluwer Academic Publishers
DT Journal
LA English
AB ***Histatins*** , a group of histidine-rich proteins in human saliva, exhibit antimicrobial activity and are therefore considered to be important in the prevention of infections in the oral cavity. Although killing of C. albicans by ***histatins*** has been extensively studied, little is known about the processes responsible for this antifungal activity. Recent studies show the requirement of metabolic activity and ATP prodn. for ***histatin*** 5 killing activity. Therefore, the goal of this study was to investigate the kinetics of ***histatin*** 5 interaction at different temps. with C. albicans wild type cells and with respiratory deficient mutants of C. albicans. Synthetic ***histatin*** 5 was labeled with fluorescein-5- isothiocyanate (FITC) and its assocn. with C. albicans cells was followed by epi-fluorescence microscopy and fluorescence confocal microscopy. At 37.degree.C, ***histatin*** 5 accumulates intracellularly, and both killing activity and uptake of unlabeled and FITC-labeled ***histatin*** 5 are time- and concn.-dependent. At 4.degree.C, no killing is obsd. and FITC- ***histatin*** 5 is only assocd. with the cytoplasmic membrane. Internalization and killing activity only occurs after cells are transferred to 37.degree.C. In addn., cellular accumulation of ***histatin*** 5 is concomitant with a moderate alteration of membrane integrity leading to the release of UV-absorbing cell components into the medium. The uptake of ***histatin*** 5, the release of UV-absorbing materials and killing of C. albicans are markedly decreased by the respiratory inhibitor sodium azide. Concomitantly, respiratory deficient mutants of C. albicans are also less susceptible to ***histatin*** 5. These results indicated that ***histatin*** 5 killing activity could be directly correlated to ***histatin*** 5 internalization. Both of these processes are prevented by modulators of cellular metabolic activity.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 22 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:914729 CAPLUS
DN 136:180481
TI The human salivary peptide ***histatin*** 5 exerts its antifungal activity through the formation of reactive oxygen species
AU Helmerhorst, Eva J.; Troxler, Robert F.; Oppenheim, Frank G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118-2392, USA
SO Proceedings of the National Academy of Sciences of the United States of America (2001), 98(25), 14637-14642 CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Previous studies have shown that the human salivary antifungal peptide ***histatin*** 5 is taken up by Candida albicans cells and assocs. intracellularly with mitochondria. The purpose of the present study was to investigate the biol. consequence of this specific subcellular targeting. ***Histatin*** 5 inhibited respiration of isolated C. albicans mitochondria as well as the respiration of intact blastoconidia in a dose- and time-dependent manner. A nearly perfect correlation was obsd. between ***histatin*** -induced inhibition of respiration and cell killing with either logarithmic- or stationary-phase cells, but stationary-phase cells were less sensitive. Because nonrespiring yeast cells are insensitive to ***histatin*** 5, the potential mechanistic relationship between ***histatin*** 5 interference with the respiratory app. and cell killing was explored by using an oxygen radical sensitive probe (dihydroethidium). Fluorimetric measurements showed that ***histatin*** 5 induced the formation of reactive oxygen species (ROS) in C. albicans cells as well as in isolated mitochondria and that ROS levels were highly correlated with cell death. In the presence of an oxygen scavenger (L-cysteine), cell killing and ROS formation were prevented. In addn., the membrane-permeant superoxide dismutase mimetic 2,2,6,6-tetramethylpiperidine-N-oxyl abolished ***histatin*** -induced ROS formation in isolated mitochondria. In contrast to ***histatin*** 5, the conventional inhibitors of the respiratory chain, sodium cyanide or sodium azide, neither induced ROS nor killed yeast cells. These data provide strong evidence for a comprehensive mechanistic model of ***histatin*** -5-provoked yeast cell death in which oxygen radical formation is the ultimate and essential step.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:887645 CAPLUS
DN 136:163989
TI P-113D, an antimicrobial peptide active against Pseudomonas aeruginosa, retains activity in the presence of sputum from cystic fibrosis patients
AU Sajjan, Umadevi S.; Tran, Linh T.; Sole, Nuria; Rovaldi, Christopher; Akiyama, Alan; Friden, Phillip M.; Forstner, Janet F.; Rothstein, David M.
CS The Hospital for Sick Children, Toronto, ON, Can.
SO Antimicrobial Agents and Chemotherapy (2001), 45(12), 3437-3444 CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Antimicrobial peptides are a source of novel agents that could be useful for treatment of the chronic lung infections that afflict cystic fibrosis (CF) patients. Efficacy depends on antimicrobial activity against the major pathogens of CF patients, e.g. Pseudomonas aeruginosa, Staphylococcus aureus, and Haemophilus influenzae, in the environment of the CF patient's

airway. We describe the in vitro efficacies of derivs. of ***histatins*** , which are histidine-rich peptides produced by the salivary glands of humans and higher primates. P-113, a peptide contg. 12 of the 24 amino acid residues of the parent mol., ***histatin*** 5, retained full antibacterial activity and had a good spectrum of activity in vitro against the prominent pathogens of CF patients. However, P-113 was not active in the presence of purulent sputum from CF patients. In contrast, P-113D, the mirror-image peptide with the amino acid residues in the D configuration, was stable in sputum, was as active as P-113 against pathogens of CF patients in the absence of sputum and retained significant activity in the presence of sputum from CF patients. Recombinant human DNase, which effectively liquefies sputum, enhanced the activity of P-113D in undiluted sputum against both exogenous (added) bacteria and endogenous bacteria. Because of its properties, P-113D shows potential as an inhalant in chronic suppressive therapy for CF patients.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:842876 CAPLUS
DN 136:384438
TI Epithelial antimicrobial peptides in host defense against infection
AU Bals, Robert
CS Ludwig-Maximilians-Universitat, Munich, Germany
SO Respiratory Research [online computer file] (2000), 1(3), 141-150 CODEN: RREEBZ; ISSN: 1465-993X URL: http://respiratory-research.com/content/1/3/141
PB BioMed Central Ltd.
DT Journal; General Review; (online computer file)
LA English
AB A review. One component of host defense at mucosal surfaces seems to be epithelium-derived antimicrobial peptides. Antimicrobial peptides are classified on the basis of their structure and amino acid motifs. Peptides of the defensin, cathelicidin, and ***histatin*** classes are found in humans. In the airways, .alpha.-defensins and the cathelicidin LL-37/hCAP-18 originate from neutrophils. .beta.-Defensins and LL-37/hCAP-18 are produced by the respiratory epithelium and the alveolar macrophage and secreted into the airway surface fluid. Beside their direct antimicrobial function, antimicrobial peptides have multiple roles as mediators of inflammation with effects on epithelial and inflammatory cells, influencing such diverse processes as proliferation, immune induction, wound healing, cytokine release, chemotaxis, protease-antiprotease balance, and redox homeostasis. Further, antimicrobial peptides qualify as prototypes of innovative drugs that might be used as antibiotics, anti-lipopolysaccharide drugs, or modifiers of inflammation.
RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:812400 CAPLUS
DN 136:63647
TI Induction of histamine release from rat peritoneal mast cells by ***histatins***
AU Yoshida, Mitsunobu; Kimura, Tomoki; Kitaichi, Kiyoyuki; Suzuki, Ryujiro; Baba, Kenji; Matsushima, Miyoko; Tatsumi, Yasuaki; Shibata, Eiji; Takagi, Kenji; Hasegawa, Takaaki; Takagi, Kenzo
CS Second Department of Internal Medicine and Laboratory Medicine, Nagoya University School of Medicine, Nagoya, 466-8560, Japan
SO Biological & Pharmaceutical Bulletin (2001), 24(11), 1267-1270 CODEN: BPBLEO; ISSN: 0918-6158
PB Pharmaceutical Society of Japan
DT Journal
LA English
AB Human salivary ***histatins*** (Hsts), which belong to a salivary polypeptide family, have potent antifungal activity against Candida albicans and Cryptococcus neoformans, and are expected to be useful as therapeutic reagents against Candida species. However, little is known about the effect of Hsts on host immune systems. Thus, we conducted a series of in vitro expts. with rat mast cells to det. whether ***histatin*** 5 (Hst 5) or ***histatin*** 8 (Hst 8) has a histamine-releasing effect on mast cells. Both Hst 5 and Hst 8 induced histamine release from rat peritoneal mast cells in a dose-dependent manner (10-9 to 10-5 M). Hst 5 had a stronger releasing effect than Hst 8. The histamine release induced by Hst 5 (10-6 M) was increased by the presence of 0.5 mM Ca2+, but decreased by 2 mM Ca2+. Alternatively, the histamine release induced by Hst 8 (10-6 M) was inhibited by the presence of Ca2+ (0.5 to 2 mM). These results suggest that Hsts have limited usefulness as therapeutic agents due to induction of histamine release from mast cells.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 26 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:698601 CAPLUS
DN 136:82177
TI A new method for the isolation of ***histatins*** 1, 3, and 5 from parotid secretion using zinc precipitation
AU Flora, Bianca; Gusman, Heloisa; Helmerhorst, Eva J.; Troxler, Robert F.; Oppenheim, Frank G.
CS Department of Periodontology and Oral Biology, Goldman School of Dental Medicine, Boston University, Boston, MA, 02118-2392, USA
SO Protein Expression and Purification (2001), 23(1), 198-206 CODEN: PEXPEJ; ISSN: 1046-5928
PB Academic Press
DT Journal
LA English
AB ***Histatins*** , a family of small-mol.-wt., histidine-rich cationic salivary proteins, have been difficult to isolate in an efficient way by conventional procedures due to their anomalous interactions with chromatog. resins. In the present study we explored the possibility of developing a new isolation procedure based on recent observations that ***histatins*** assoc. with various metal ions, including zinc. Since soly. studies showed that ***histatin*** 5 forms ppts. with zinc under alk. conditions, we investigated whether this characteristic could be exploited for the preparative isolation of ***histatins*** from salivary secretions. A fast and efficient two-step procedure was developed using zinc pptn. of ***histatins*** from human parotid secretion followed by final purifn. using reversed-phase high-performance liq. chromatog. (HPLC). Anal. of zinc ppts. by Tricine-SDS-PAGE, cationic PAGE, HPLC, and mass spectrometry revealed the presence of the three major ***histatins*** , 1, 3, and 5, as well as statherin. The ***histatin*** yield obtained by the pptn. step was approx. 90%. Therefore, zinc pptn. of ***histatins*** from glandular salivary secretions is a novel, rapid, and effective means for the isolation of these proteins. (c) 2001 Academic Press.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 27 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:634990 CAPLUS
DN 135:300181
TI The molecular interaction of human salivary ***histatins*** with polyphenolic compounds

AU Wroblewski, Karol; Muhandiram, Ranjith; Chakrabartty, Avi; Bennick, Anders
CS Department of Biochemistry, University of Toronto, Toronto, ON, M5S 1A8, Can.
SO European Journal of Biochemistry (2001), 268(16), 4384-4397
CODEN: EJBCAI; ISSN: 0014-2956
PB Blackwell Science Ltd.
DT Journal
LA English
AB Dietary tannins are polyphenols that are effectively pptd. by salivary ***histatins*** (Hsts), a novel family of tannin binding proteins. Epigallocatechin gallate (EGCG), a flavan-3-ol ester related to condensed tannins (polymd. products of flavan-3-ols), and pentagalloyl glucose (PGG), a hydrolyzable tannin, were used to evaluate the mol. nature of Hst-polyphenol interaction. NMR demonstrated that Hst5, a representative Hst, bound to EGCG in a hydrophobic manner via basic and arom. residues. In contrast, proline plays a dominant role in polyphenol binding to other tannin pptg. proteins. The role of basic and arom. amino acids in EGCG binding was investigated using a series of modified Hsts in each of which one type of amino acid was substituted by Ala. EGCG bound to all modified Hsts, but the binding was diminished. Optimal EGCG binding also depended on the primary structure, as a polypeptide with randomized Hst5 sequence showed significantly diminished interaction with EGCG. Sol. EGCG/Hst5 complexes contg. up to seven mols. of EGCG per mol. of Hst5 had a 1-mM dissocn. const. In contrast to EGCG, PGG formed small sol. complexes with Hst5 consisting of only one mol. each of PGG and Hst5, as demonstrated by anal. ultracentrifugation. These complexes became insol. upon binding of addnl. mols. of PGG. Diminished PGG binding was seen to a peptide with a Hst5 randomized sequence showing the importance of the primary structure. Hsts may serve to form insol. complexes with tannins thereby preventing their absorption from the intestines and potentially harmful biol. effects. In contrast the much weaker interaction with EGCG may allow its uptake into the organism and exploitation of its antioxidant effect.
RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 28 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:585988 CAPLUS
DN 135:285597
TI Antifungal activity of ***histatin*** -5 against non-albicans Candida species
AU Nikawa, H.; Jin, C.; Fukushima, H.; Makihira, S.; Hamada, T.
CS Department of Prosthetic Dentistry, Hiroshima University Faculty of Dentistry, Hiroshima, 734-8553, Japan
SO Oral Microbiology and Immunology (2001), 16(4), 250-252
CODEN: OMIMEE; ISSN: 0902-0055
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB Fungicidal effects of ***histatin*** -5 against 26 oral isolates belonging to 5 non-albicans Candida species were examd. 50 .mu.M of ***histatin*** -5 killed more than 95% of Candida tropicalis and Candida guilliermondii isolates and more than 90% of Candida parapsilosis, and Candida krusei. However, Candida glabrata was less sensitive to the peptide (mean 62.9%). These results, taken together, demonstrated that ***histatin*** -5 possessed the fungicidal activity against Candida species other than C. glabrata.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 29 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:581749 CAPLUS
DN 135:157726
TI Medical device coated with antimicrobial peptides
IN Van Nieuw, Amerongen Arie; Veerman, Engelmundus Cornelis Ignatius; Van't Hof, Willem
PA Am-Pharma B.V., Neth.
SO PCT Int. Appl., 22 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 2001056627 A1 20010809 WO 2001-NL19 20010112 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI NL 2000-1008734 A 20000112
AB Described is a medical device for application onto or into a body of a patient, coated with one or more naturally occurring peptides or proteins or synthetic peptides and analogs thereof having antimicrobial activity. The antimicrobial peptides and proteins are preferably chosen from the group, consisting of cystatin-derived peptides, ***histatin*** -derived peptides, lactoferrin-derived peptides and specific proteinase inhibitors.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 30 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:564773 CAPLUS
DN 135:148255
TI Nucleic acids and their encoded polypeptides from human tissues
IN Tang, Y. Tom; Liu, Chenghua; Zhou, Ping; Qian, Xiaohong B.; Wang, Zhiwei; Chen, Rui-Hong; Asundi, Vinod; Cao, Yicheng; Drmanac, Radoje A.; Zhang, Jie; Werhman, Tom
PA Hyseq, Inc., USA
SO PCT Int. Appl., 1275 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 91 PATENT NO. KIND DATE APPLICATION NO. DATE --- ---------- ---- -------- ---------- --------
PI WO 2001054477 A2 20010802 WO 2001-US2687 20010125 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 2001033041 A5 20010807 AU 2001-33041 20010125
PRAI US 2000-491404 A 20000125 US 2000-617746 A 20000717 US 2000-631451 A 20000803 US 2000-663870 A 20000915 WO 2001-US2687 W 20010125
AB The present invention provides a collection or library of 1009 nucleic acid contig sequences assembled from expressed sequence tag or cDNA libraries isolated mainly by sequencing by hybridization (SBH), std. PCR, Sanger sequencing techniques, and in some cases, sequences obtained form one or more public databases. Tissue sources and nearest neighbor homologies are provided. The invention also relates to the proteins encoded by

such polynucleotides, along with therapeutic, diagnostic and research utilities for these polynucleotides and proteins.

L3 ANSWER 31 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:522555 CAPLUS
DN 135:207175
TI Molecular dynamics simulation of the antimicrobial salivary peptide ***histatin*** -5 in water and in trifluoroethanol: A microscopic description of the water destructuring effect
AU Iovino, M.; Falconi, M.; Marcellini, A.; Desideri, A.
CS National Institute for the Physics of Matter (INFM) and Department of Biology, University of Rome "Tor Vergata", Rome, 00133, Italy
SO Journal of Peptide Research (2001), 58(1), 45-55 CODEN: JPERFA; ISSN: 1397-002X
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB The results of a 520 ps mol. dynamics simulation of ***histatin*** -5, a small peptide present in human saliva and possessing antimicrobial activity, dissolved in water and in 2,2,2-trifluoroethanol, are reported. The simulations indicate that ***histatin*** -5 is destabilized in water and begins to unfold after 250 ps, while in org. solvent it maintains a regular secondary structure throughout the trajectory. Anal. of the peptide-solvent hydrogen bonds indicates that 2,2,2-trifluoroethanol is a poorer proton acceptor than water. The fluorine atom of the alc. is almost never engaged in a hydrogen bond and the org. solvent interacts mainly with the peptide through its hydroxyl group. For some residues, anal. of the solvent residence time indicated longer values for 2,2,2-trifluoroethanol than for water. The most striking difference is related to the no. of times the solvent enters and leaves the first coordination shell of the peptide. This value was more than one order of magnitude higher for water than for the alc., suggesting that this may be the main cause of .alpha.-helix destabilization perpetrated by water.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 32 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:473713 CAPLUS
DN 135:209872
TI Porphyromonas gingivalis gingipain-R enhances interleukin-8 but decreases gamma interferon-inducible protein 10 production by human gingival fibroblasts in response to T-cell contact
AU Oido-Mori, Mari; Rezzonico, Roger; Wang, Pao-Li; Kowashi, Yusuke; Dayer, Jean-Michel; Baehni, Pierre C.; Chizzolini, Carlo
CS Department of Preventive Dentistry, School of Dental Medicine, University of Geneva, Geneva, 1211/14, Switz.
SO Infection and Immunity (2001), 69(7), 4493-4501 CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
AB Proteases produced by Porphyromonas gingivalis, an oral pathogen, are considered important virulence factors and may affect the responses of cells equipped with proteinase-activated receptors. The aim of this study was to investigate the effect of the arginine-specific cysteine protease gingipain-R produced by P. gingivalis on chemokine prodn. by human gingival fibroblasts (HGF) and the effect of gingipain-R treatment on the subsequent contact-dependent activation of HGF by T cells. HGF incubated in the presence of purified 47-kDa gingipain-R showed increased levels of interleukin-8 (IL-8) mRNA. Cyclooxygenase-2 (COX-2) mRNA was also induced. Further exposure of HGF to activated T cells resulted in the dose- and time-dependent enhancement of IL-8 transcription and release. T-cell membrane-bound tumor necrosis factor (TNF) was the ligand inducing IL-8 prodn. by HGF, since TNF neutralization abrogated HGF responses to T-cell contact. The enhanced IL-8 release was due, at least in part, to prostaglandin-E2 prodn., which was mostly blocked by indomethacin. Gingipain-R proteolytic activity was required since heat inactivation, specific synthetic protease inhibitors, and the natural substrate competitor ***histatin*** 5 abrogated its effects. The enhanced prodn. of IL-8 in response to T-cell contact was specific since monocyte chemotactic protein-1 (MCP-1) prodn. was unaffected while interferon-gamma-inducible protein-10 (IP-10) was inhibited. The sum of these activities may result in the recruitment of differential cell types to sites of inflammation since IL-8 preferentially recruits neutrophils and IP-10 attracts activated T cells and may be relevant to the pathogenesis of periodontitis.
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 33 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:462667 CAPLUS
DN 135:192715
TI Effects of ***histatin*** 5 and derived peptides on Candida albicans
AU Ruissen, Anita L. A.; Groenink, Jasper; Helmerhorst, Eva J.; Walgreen-Weterings, Els; Van't Hof, Wim; Veerman, Enno C. I.; Nieuw Amerongen, Arie V.
CS Department of Dental Basic Sciences, Section of Oral Biochemistry, Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam, 1081 BT, Neth.
SO Biochemical Journal (2001), 356(2), 361-368 CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English
AB Three anti-microbial peptides were compared with respect to their killing activity against Candida albicans and their ability to disturb its cellular and internal membranes. ***Histatin*** 5 is an anti-fungal peptide occurring naturally in human saliva, while dhvar4 and dhvar5 are variants of its active domain, with increased anti-microbial activity. Dhvar4 has increased amphipathicity compared with ***histatin*** 5, whereas dhvar5 has amphipathicity comparable with that of ***histatin*** 5. All three peptides caused depolarization of the cytoplasmic and/or mitochondrial membrane, indicating membranolytic activity. For the variant peptides both depolarization and killing occurred at a faster rate. With FITC-labeled peptides, no assocn. with the cytoplasmic membrane was obsd., contradicting the formation of permanent transmembrane multimeric peptide pores. Instead, the peptides were internalized and act on internal membranes, as demonstrated with mitochondrion- and vacuole-specific markers. In comparison with ***histatin*** 5, the variant peptides showed a more destructive effect on mitochondria. Entry of the peptides and subsequent killing were dependent on the metabolic state of the cells. Blocking of the mitochondrial activity led to complete protection against ***histatin*** 5 activity, whereas that of dhvar4 was hardly affected and that of dhvar5 was affected only intermediately.
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 34 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:395213 CAPLUS
DN 138:68503
TI Characterization of ***histatin*** 5 with respect to amphipathicity, hydrophobicity, and effects on cell and mitochondrial membrane integrity excludes a candidacidal

mechanism of pore formation. [Erratum to document cited in CA134:322286]
AU Helmerhorst, Eva J.; van't Hof, Wim; Breeuwer, Pieter; Veerman, Enno C. I.; Abee, Tjakko; Troxler, Robert F.; Nieuw Amerongen, Arie V.; Oppenheim, Frank G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118, USA
SO Journal of Biological Chemistry (2001), 276(20), 17620 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB The correct spelling of the first author's name is Eva J. Helmerhorst.

L3 ANSWER 35 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:386816 CAPLUS
DN 135:235949
TI Clinical and microbial evaluation of a ***histatin*** -containing mouthrinse in humans with experimental gingivitis
AU Mickels, Nancy; McManus, Colleen; Massaro, Joseph; Friden, Phillip; Braman, Virginia; D'Agostino, Ralph; Oppenheim, Frank; Warbington, Martha; Dibart, Serge; Van Dyke, Thomas
CS Boston University Goldman School of Dental Medicine, Boston, MA, USA
SO Journal of Clinical Periodontology (2001), 28(5), 404-410 CODEN: JCPEDZ; ISSN: 0303-6979
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB Objective: P-113, a 12 amino acid ***histatin*** -based peptide, was evaluated in a mouthrinse formulation for safety, prevention of the development of exptl. gingivitis, and for its effects on periodontal flora. Method: 159 periodontally healthy subjects abstained from oral hygiene procedures and self-administered either 0.005%, 0.01%, 0.05% P-113 or placebo mouthrinse formulations twice daily over a four week treatment period. During this time, the safety, anti-plaque, and anti-gingivitis effects of P-113 were evaluated. Results: There was a significant redn. in plaque ($p=0.046$) and a redn. in gingivitis ($p=0.086$) for subjects using 0.01% P-113 mouthrinse. Significantly more subjects in the 0.01% and 0.05% treatment groups showed a small increase in plaque index of <0.25 as compared to the placebo group ($p<0.05$). Similar trends were noted for changes in the % of sites with bleeding on probing in the 0.01% P-113 group. There were no treatment-related adverse events, and there were no adverse shifts in supragingival microflora during the study. Conclusion: These data suggest that P-113 mouthrinse is safe and reduces plaque, gingivitis and gingival bleeding in the human exptl. gingivitis model.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 36 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:374770 CAPLUS
DN 135:119463
TI Released ATP is an extracellular cytotoxic mediator in salivary ***histatin*** 5-induced killing of Candida albicans
AU Koshlukova, Svetlana E.; Araujo, Marcelo W. B.; Baev, Didi; Edgerton, Mira
CS Department of Oral Biology, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Infection and Immunity (2000), 68(12), 6848-6856 CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
AB Salivary ***histatins*** (Hsts) are antifungal peptides with promise as therapeutic agents against candidiasis. Hst 5 kills the fungal pathogen Candida albicans via a mechanism that involves release of cellular ATP in the absence of cytolysis. Here, the authors demonstrate that released ATP has a further role in Hst 5 killing. Incubation of the cells with ATP analogs induced cell death, and addn. of the ATP scavenger apyrase to remove extracellular ATP released during Hst 5 treatment resulted in a redn. in cell killing. Expts. using anaerobically grown C. albicans with decreased susceptibility to Hst 5 confirmed that depletion of cellular ATP as a result of ATP efflux was not sufficient to cause cell death. In contrast to Hst-susceptible aerobic cultures, anaerobically grown cells were not killed by exogenously applied ATP. These findings established that Hst binding, subsequent entry into the cells, and ATP release precede the signal for cytotoxicity, which is mediated by extracellular ATP. In a higher-eukaryote paradigm, released ATP acts as a cytotoxic mediator by binding to membrane nucleotide P2X receptors. Based on a pharmacol. profile and detection of a C. albicans 60-kDa membrane protein immunoreactive with antibody to P2X7 receptor, we propose that released ATP in response to Hst 5 activates candidal P2X7-like receptors to cause cell death.
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 37 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:319291 CAPLUS
DN 135:89715
TI Anticandida activity is retained in P-113, a 12-amino-acid fragment of ***histatin*** 5
AU Rothstein, David M.; Spacciapoli, Peter; Tran, Linh T.; Xu, Tao; Roberts, F. Donald; Dalla Serra, Mauro; Buxton, Deborah K.; Oppenheim, Frank G.; Friden, Phillip
CS Periodontix, Inc., Watertown, MA, USA
SO Antimicrobial Agents and Chemotherapy (2001), 45(5), 1367-1373 CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Through the anal. of a series of 25 peptides composed of various portions of the ***histatin*** 5 sequence, we have identified P-113, a 12-amino-acid fragment of ***histatin*** 5, as the smallest fragment that retains anticandidal activity comparable to that of the parent compd. Amidation of the P-113 C terminus increased the anticandidal activity of P-113 .apprx.2-fold. The 3 histidine residues could be exchanged for 3 hydrophobic residues, with the fragment retaining anticandidal activity. However, the change of .gtoreq.2 of the 5 basic (lysine and arginine) residues to uncharged residues resulted in a substantial loss of anticandidal activity. A synthetic D-amino-acid analog, P-113D, was as active against Candida albicans as the L-amino-acid form. In vitro MIC tests in low-ionic-strength medium showed that P-113 has potent activity against Candida albicans, Candida glabrata, Candida parapsilosis, and Candida tropicalis. These results identify P-113 as a potential antimicrobial agent in the treatment of oral candidiasis.
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 38 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:287562 CAPLUS
DN 135:90398
TI New in vitro model for the acquired enamel pellicle: pellicles formed from whole saliva show inter-subject consistency in protein composition and proteolytic fragmentation patterns

AU Lamkin, M. S.; Migliari, D.; Yao, Y.; Troxler, R. F.; Oppenheim, F. G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118, USA
SO Journal of Dental Research (2001), 80(1), 385-388 CODEN: JDREAF; ISSN: 0022-0345
PB International Association for Dental Research
DT Journal
LA English
AB The present investigation was undertaken to investigate the variability of proteins in whole saliva which adsorb to hydroxyapatite and are thus likely to be precursors of the acquired enamel pellicle. Whole-saliva proteins from 18 subjects were absorbed to hydroxyapatite, and the gel filtration patterns of released proteins revealed 4 major peaks and 3 minor peaks eluting between the major peaks. Amino acid anal. indicated that minor peaks contained fragments of proteins in major peaks, and this was confirmed by sequence anal. Major peaks comprised 95% and minor peaks comprised 5% of protein absorbed to hydroxyapatite, suggesting a limited proteolytic capacity of whole saliva. HPLC elution patterns of components in minor peaks suggested that proteolysis is not totally random but is an orderly and consistent process. These studies suggest that whole saliva may be suitable as a model system for the investigation of post-secretory modifications of salivary proteins important for the formation of the acquired enamel pellicle.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 39 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:287379 CAPLUS
DN 135:3508
TI Electron-microscopic demonstration of proline-rich proteins, statherin, and ***histatins*** in acquired enamel pellicles in vitro
AU Schupbach, P.; Oppenheim, F. G.; Lendenmann, U.; Lamkin, M. S.; Yao, Y.; Guggenheim, B.
CS Institute of Oral Microbiology and General Immunology, Center for Dental and Oral Medicine and Maxillofacial Surgery, University of Zurich, Zurich, CH-8028, Switz.
SO European Journal of Oral Sciences (2001), 109(1), 60-68 CODEN: EJOSFY; ISSN: 0909-8836
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB Proline-rich proteins (PRPs), ***histatins*** , and statherin are salivary proteins that exhibit high affinities for hydroxyapatite surfaces. In vitro expts. with parotid, submandibular/sublingual or whole saliva have shown these proteins to adsorb selectively to tooth surfaces. This investigation focused on the histomorphol. identification of PRPs, ***histatins*** , and statherin in acquired enamel pellicles. Synthetic hydroxyapatite or bovine enamel were exposed to glandular secretions, and whole saliva and pellicle precursor proteins were identified immunohistol. by electron microscopy. Results obtained by back-scattered SEM showed these proteins to be present in pellicles. Pellicles displayed a distinct structure consisting of a sponge-like meshwork of microglobules. Interconnections between structural elements were identified in submandibular/sublingual and whole saliva pellicles only. Transmission electron microscopy of pellicles formed on bovine enamel surfaces revealed a tendency for preferential localization of precursor proteins within the protein film. Since the data showed the presence of pellicle precursors in pellicles derived both from glandular secretions and from whole saliva, it is likely that PRPs, ***histatins*** , and statherin are integral components of acquired enamel pellicles in vivo.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 40 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:215850 CAPLUS
DN 134:307137
TI Salivary ***histatin*** 5 is an inhibitor of both host and bacterial enzymes implicated in periodontal disease
AU Gusman, Heloisa; Travis, James; Helmerhorst, Eva J.; Potempa, Jan; Troxler, Robert F.; Oppenheim, Frank G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118-2392, USA
SO Infection and Immunity (2001), 69(3), 1402-1408 CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
AB One of the salient features of periodontitis and gingivitis is the increase in the levels of bacterial and host-derived proteolytic enzymes in oral inflammatory exudates. This study evaluated the potential of ***histatin*** 5, a 24-residue histidine-rich salivary antimicrobial protein, to inhibit these enzymes. Using biotinylated gelatin as a substrate, ***histatin*** 5 was found to inhibit the activity of the host matrix metalloproteinases MMP-2 and MMP-9 with 50% inhibitory concns. (IC50s) of 0.57 and 0.25 .mu.M, resp. To localize the domain responsible for this inhibition, three peptides contg. different regions of ***histatin*** 5 were synthesized and tested as inhibitors of MMP-9. Peptides comprising residues 1 to 14 and residues 4 to 15 of ***histatin*** 5 showed much lower inhibitory activities (IC50, 21.4 and 20.5 .mu.M, resp.), while a peptide comprising residues 9 to 22 showed identical activity to ***histatin*** 5 against MMP-9. These results point to a functional domain localized in the C-terminal part of ***histatin*** 5. To evaluate the effect of ***histatin*** 5 on bacterial proteases, a detailed characterization of ***histatin*** 5 inhibition of gingipains from Porphyromonas gingivalis was carried out using purified Arg- and Lys-specific enzymes. Kinetic anal. of the inhibition of the Arg-gingipain revealed that ***histatin*** 5 is a competitive inhibitor, affecting only the Km with a Ki of 15 .mu.M. In contrast, inhibition of Lys-gingipain affected both the Km and Vmax, suggesting that both competitive and noncompetitive competitive processes underlie this inhibition. The inhibitory activity of ***histatin*** 5 against host and bacterial proteases at physiol. concns. points to a new potential biol. function of ***histatin*** in the oral cavity.
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 41 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:166538 CAPLUS
DN 134:322286
TI Characterization of ***histatin*** 5 with respect to amphipathicity, hydrophobicity, and effects on cell and mitochondrial membrane integrity excludes a candidacidal mechanism of pore formation
AU Helmerhorst, Eva J.; Van't Hof, Wim; Breeuwer, Pieter; Veerman, Enno C. I.; Abee, Tjakko; Troxler, Robert F.; Nieuw Amerongen, Arie V.; Oppenheim, Frank G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118, USA
SO Journal of Biological Chemistry (2001), 276(8), 5643-5649 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal

LA English
AB ***Histatin*** 5 is a 24-residue peptide from human saliva with antifungal properties. We recently demonstrated that ***histatin*** 5 translocates across the yeast membrane and targets to the mitochondria, suggesting an unusual antifungal mechanism. The present study used specifically designed synthetic analogs of ***histatin*** 5 to elucidate the role of peptide amphipathicity, hydrophobicity, and the propensity to adopt .alpha.-helical structures in relation to membrane permeabilization and fungicidal activity. Studies included CD measurements, evaluation of the effects on the cytoplasmic transmembrane potential and on the respiration of isolated mitochondria, and anal. of the peptide hydrophobicity/amphipathicity relationship. The 14-residue synthetic peptides used were dh-5, comprising the functional domain of ***histatin*** 5, and dhvar1 and dhvar4, both designed to maximize amphipathic characteristics. The results obtained show that the amphipathic analogs exhibited a high fungicidal activity, a high propensity to form an .alpha.-helix, dissipated the cytoplasmic transmembrane potential, and uncoupled the respiration of isolated mitochondria, similar to the pore-forming peptide PGLa (Peptide with N-terminal Glycine and C-terminal Leucine-amide). In contrast, ***histatin*** 5 and dh-5 showed fewer or none of these features. The difference in these functional characteristics between ***histatin*** 5 and dh-5 on the one hand and dhvar1, dhvar4, and PGLa on the other hand correlated well with their predicted affinity for membranes based on hydrophobicity/amphipathicity anal. These data indicate that the salivary peptide ***histatin*** 5 exerts its antifungal function through a mechanism other than pore formation.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 42 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:166149 CAPLUS
DN 134:323334
TI Salivary ***histatin*** 5 and human neutrophil defensin 1 kill Candida albicans via shared pathways
AU Edgerton, Mira; Koshlukova, Svetlana E.; Araujo, Marcelo W. B.; Patel, Rashmi C.; Dong, Jin; Bruenn, Jeremy A.
CS Departments of Oral Biology, Restorative Dentistry, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Antimicrobial Agents and Chemotherapy (2000), 44(12), 3310-3316 CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Salivary ***histatins*** are a family of basic histidine-rich proteins in which therapeutic potential as drugs against oral candidiasis is apparent, considering their potent in vitro antifungal activity and lack of toxicity to humans. ***Histatin*** 5 (Hst 5) kills the fungal pathogen Candida albicans via a mechanism that involves binding to specific sites on the yeast cell membrane and subsequent release of cellular ATP in the absence of cytolysis. We explored the killing pathway activated by Hst 5 and compared it to those activated by other antifungal agents. The candidacidal activity of human neutrophil defensin 1 (HNP-1) shared very similar features to Hst 5 cytotoxic action with respect to active concns. and magnitude of induction of nonlytic ATP efflux, depletion of intracellular ATP pools, and inhibitor profile. Hst 5 and HNP-1 are basic proteins of about 3 kDa; however, they have unique primary sequences and soln. structures that cannot explain how these two mols. act so similarly on C. albicans to induce cell death. Our finding that HNP-1 prevented Hst 5 binding to the candidal Hst 5 binding protein suggests that the basis for the overlapping actions of these two naturally occurring antimicrobial proteins may involve interactions with shared yeast components.
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 43 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:150250 CAPLUS
DN 134:322547
TI Salivary ***histatin*** 5 is a potent competitive inhibitor of the cysteine proteinase clostripain
AU Gusman, H.; Grogan, J.; Kagan, H. M.; Troxler, R. F.; Oppenheim, F. G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118-2392, USA
SO FEBS Letters (2001), 489(1), 97-100 CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
AB ***Histatin*** 5 is a low mol. wt. salivary protein which is known to exhibit inhibitory activity against several proteinases, including the cysteine proteinases gingipains. The purpose of this study was to characterize the effect of salivary ***histatin*** on the proteolytic activity of the cysteine proteinase clostripain derived from the pathogen Clostridium histolyticum. Using a synthetic nitroanilide substrate, we studied in detail the inhibition of clostripain by ***histatin*** 5 and compared the effect of this peptide to that of leupeptin, a known competitive inhibitor of clostripain. It was found that the concn. of ***histatin*** 5 required to inhibit 50% of clostripain activity was 23.6.+-.1.6 nM. Kinetic anal. revealed that ***histatin*** 5 is a competitive inhibitor of clostripain with an inhibition const. (Ki) of 10 nM. The Ki for the inhibition of clostripain activity against nitroanilide substrate by leupeptin was found to be 60 nM, significantly higher than that of ***histatin*** 5. Thus, ***histatin*** 5 inhibits clostripain more effectively than leupeptin and other cysteine protease inhibitors studied here. No significant proteolysis of ***histatin*** 5 was obsd. when ***histatin*** 5 was incubated at physiol. concns. with clostripain. The potent inhibition of clostripain by ***histatin*** 5 points towards the possibility that this protein may prevent establishment of clostridial infections and therefore may have significant potential for the treatment of diseases assocd. with this enzyme.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 44 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:150213 CAPLUS
DN 134:325127
TI Zinc and copper bind to unique sites of ***histatin*** 5
AU Grogan, J.; McKnight, C. J.; Troxler, R. F.; Oppenheim, F. G.
CS Department of Periodontology and Oral Biology, Boston University Medical Center, Boston, MA, 02118, USA
SO FEBS Letters (2001), 491(1,2), 76-80 CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
AB Metal binding has been suggested to be relevant in the antifungal and antibacterial mechanism of ***histatin*** 5, a human salivary protein. Proton NMR spectra were obtained to investigate the specificity of metal binding to the seven histidyl, one aspartyl and one glutamyl amino acid side-chains of ***histatin*** 5 in aq. solns. Three C.epsilon.1-H histidyl and the C.gamma.-H glutamyl resonances of ***histatin*** 5 were selectively altered in spectra of solns. contg. three equiv. of zinc.

Copper binding to ***histatin*** 5 resulted in a reduced intensity of C.beta.-H aspartyl resonances, while no evidence for calcium binding was found. These results indicate that zinc binding to ***histatin*** 5 involves His-15 present within the -H-E-X-X-H- zinc binding motif, and copper binding occurs within the N-terminal D-S-H-, ATCUN motif.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 45 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:98289 CAPLUS
DN 134:338097
TI Synergistic effects of low doses of ***histatin*** 5 and its analogues on amphotericin B anti-mycotic activity
AU Van't Hof, Wim; Reijnders, Ingrid M.; Helmerhorst, Eva J.; Walgreen-Weterings, Els; Simoons-Smit, Ina M.; Veerman, Enno C. I.; Nieuw Amerongen, Arie V.
CS Academic Centre for Dentistry, Vrije Universiteit, Amsterdam, Neth.
SO Antonie van Leeuwenhoek (2000), 78(2), 163-169 CODEN: ALJMAO; ISSN: 0003-6072
PB Kluwer Academic Publishers
DT Journal
LA English
AB The increase in the use of antifungal agents for prophylaxis and therapy has led to the development of antifungal drug resistance. Drug combinations may prevent or delay resistance development. The aim of the present study was to investigate whether naturally and designed cationic antifungal peptides act synergistically with commonly used antimycotics. No enhanced activity was found upon addn. of dhvar4, a designed analog of the human salivary peptide ***histatin*** 5, or PGLa to fluconazole or 5-flucytosine, resp. In contrast, strong synergism of amphotericin B with the peptides was found against several Aspergillus, Candida, and Cryptococcus strains, and against an amphotericin B-resistant C. albicans lab. mutant in the standardized broth microdilution assays according to the NCCLS std. method M27-T. Amphotericin B showed synergism with dhvar5, another designed analog of ***histatin*** 5, and with magainin 2 against all 7 tested strains. Combinations of amphotericin B with ***histatin*** 5, dhvar4, and PGLa showed synergism against 4 of the 7 strains. The growth inhibitory activity of amphotericin B was enhanced by sub-MIC concns. of peptide, but its hemolytic activity remained unaffected, suggesting that its cytotoxicity to host cells was not increased and that peptides may be suitable candidates for combination therapy.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 46 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:97979 CAPLUS
DN 134:249000
TI Determination of the human salivary peptides ***histatins*** 1, 3, 5 and statherin by high-performance liquid chromatography and by diode-array detection
AU Castagnola, M.; Congiu, D.; Denotti, G.; Di Nunzio, A.; Fadda, M. B.; Melis, S.; Messana, I.; Misiti, F.; Murtas, R.; Olianas, A.; Piras, V.; Pittau, A.; Puddu, G.
CS Section of Biochemistry and Molecular Biology of the Department of Sciences Applied to Biosystems, Cagliari University, Monserrato, Cagliari, 09042, Italy
SO Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 751(1), 153-160 CODEN: JCBBEP; ISSN: 0378-4347
PB Elsevier Science B.V.
DT Journal
LA English
AB A reversed-phase HPLC method with diode-array detection for the quantification of several human salivary peptides is described. Sample pretreatment consisted of the acidification of whole saliva by phosphate buffer. This treatment produced pptn. of mucins, .alpha.-amylases and other high-mol.-mass salivary proteins, simultaneous inhibition of intrinsic protease activities and redn. of sample viscosity. Direct HPLC anal. by diode-array detection of the resulting acidic sample allowed one to quantify ***histatin*** 1, ***histatin*** 3, ***histatin*** 5, statherin, as well as uric acid, in normal subjects. Also, the groups of peaks pertaining to proline-rich proteins and cystatins were tentatively identified. The method can be useful in assessing the concn. of salivary peptides from normal subjects and from patients suffering oral and/or periodontal diseases.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 47 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:95629 CAPLUS
DN 134:337253
TI Is salivary ***histatin*** 5 a metallopeptide?
AU Gusman, H.; Lendenmann, U.; Grogan, J.; Troxler, R. F.; Oppenheim, F. G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118-2392, USA
SO Biochimica et Biophysica Acta (2001), 1545(1-2), 86-95 CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal
LA English
AB ***Histatins*** are small histidine-rich salivary polypeptides which exhibit antimicrobial activity against Candida albicans. This antimicrobial activity has been ascribed in part to a high content of basic amino acids. However, unlike most other antimicrobial proteins ***histatins*** have a high content of histidine, tyrosine and acidic amino acids known to participate in metal ion coordination. This study was conducted to test whether ***histatin*** 5 could bind zinc and copper which are metals present in salivary secretions and whole saliva. Phys. binding parameters and spectral properties of zinc- and copper-***histatin*** complexes were investigated in order to obtain direct evidence of these interactions. A spectrophotometric competition assay using the metallochromic indicator murexide showed that ***histatin*** 5 dissocs. metal indicator complexes contg. zinc or copper ions. Absorption spectra of ***histatin*** 5 at increasing copper chloride concns. resulted in higher absorbance in the 230-280 nm wavelength range and this spectral change was satd. at a peptide:metal molar ratio of approx. 1:1. A corresponding band was obsd. in the visible range of the spectrum with a max. and molar extinction coeff. corresponding to that of copper binding to an ATCUN motif. Quant. assessment of zinc and copper binding to ***histatin*** 5 using isothermal titrn. calorimetry revealed at least one high affinity site for each metal, with binding consts. of 1.2.times.105 and 2.6.times.107 M-1, resp. These results indicate that ***histatin*** 5 exhibits metallopeptide-like properties. The precise biol. significance of this has not yet been established but ***histatins*** may contribute significantly to salivary metal binding capacity.
RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 48 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:51863 CAPLUS
DN 134:110031

TI Antimicrobial peptides and peptide antibiotics
AU Bals, Robert
CS Medizinische Klinik und Poliklinik I, Schwerpunkt Pneumologie, Klinikum der Universitat Munchen, Grosshadern, Munchen, D-81773, Germany
SO Medizinische Klinik (Muenchen) (2000), 95(9), 496-502 CODEN: MEKLA7; ISSN: 0723-5003
PB Urban & Vogel Medien und Medizin Verlagsgesellschaft mbH
DT Journal; General Review
LA German
AB A review with 54 refs. is given focussing on the biol. of antimicrobial peptides as well as their potential as drugs. Antimicrobial peptides are naturally occurring antibiotics. As part of the innate immune system of vertebrates they have direct antimicrobial function. Further, they can act as mediators of inflammation. Their antimicrobial spectrum covers gram-pos. and -neg. bacteria as well as fungi and certain viruses. Based on their structure, antimicrobial peptides can be divided into several families. Peptides of the defensin, cathelicidin, and ***histatin*** families were isolated from humans, where they were found in defense cells, such as macrophages or neutrophils, as well as in epithelial cells. Decreased prodn. of antimicrobial peptides is assocd. with immune deficiencies. Further, lung disease in cystic fibrosis may be linked to the dysfunction of antimicrobial peptides. Based on naturally occurring antimicrobial peptides, derivates of these mols. were developed as innovative antibiotic drugs.
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 49 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:894827 CAPLUS
DN 134:277030
TI Complexation analysis of the antimicrobial salivary ***histatin*** peptides
AU Brewer, Dyanne; Lajoie, Gilles
CS Guelph-Waterloo Center for Graduate Work in Chemistry and Biochemistry, Department of Chemistry, University of Waterloo, Waterloo, ON, N2L 3G1, Can.
SO Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 744-745. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Publisher: Kluwer Academic Publishers, Dordrecht, Neth. CODEN: 69ATHX
DT Conference
LA English
AB ***Histatins*** are a family of histidine-rich peptides found in human saliva that possess potent antimicrobial activity. Their mode of action is as yet unclear. The two most potent ***histatins*** are the 32 amino acid long ***histatin*** 3 (H3), and ***histatin*** 5 (H5) which corresponds to the first 24 residues of H3. The seven histidines in these peptides suggests the potential for complexation with various metal ions. The formation of stable ***histatin*** -metal complexes could play a role in biol. activity. The coordination properties of H3 and H5 with various metal ions was examd. by ES-MS. Results suggest that H3 and H5 are capable of sequestering metal ions from microorganisms.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 50 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:857931 CAPLUS
DN 135:4316
TI ***Histatin*** 5 inhibits inflammatory cytokine induction from human gingival fibroblasts by Porphyromonas gingivalis
AU Imatani, T.; Kato, T.; Minaguchi, K.; Okuda, K.
CS Oral Health Science Center, Tokyo Dental College, Chiba, 261-8502, Japan
SO Oral Microbiology and Immunology (2000), 15(6), 378-382 CODEN: OMIMEE; ISSN: 0902-0055
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB Porphyromonas gingivalis is a gram-neg. rod assocd. with the progression of human periodontal disease. It has been demonstrated that outer-membrane proteins as well as lipopolysaccharides from P. gingivalis ATCC 53977 can induce interleukin 6 (IL-6) and IL-8 from the cells of the periodontium in vitro. But, they cannot induce IL-1 and tumor necrosis factor-.alpha. from the cells. In the present study, we studied the effects of salivary protein on cytokine induction from human gingival fibroblasts by P. gingivalis outer-membrane protein. ***Histatin*** 5 suppressed the IL-6 and IL-8 induction by P. gingivalis outer-membrane protein. This activity was more effective when outer-membrane protein was incubated with ***histatin*** 5 before addn. to the cell culture. The present study indicates that ***histatin*** 5 restrains induction of inflammatory cytokines by periodontal pathogens and that ***histatin*** is one of the salivary proteins responsible for this activity.
RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 51 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:785674 CAPLUS
DN 134:71879
TI Divergent solid-phase synthesis and candidacidal activity of MUC7 D1, a 51-residue histidine-rich N-terminal domain of human salivary mucin MUC7
AU Satyanarayana, J.; Situ, H.; Narasimhamurthy, S.; Bhayani, N.; Bobek, L. A.; Levine, M. J.
CS Department of Oral Biology, State University of New York at Buffalo, Buffalo, NY, 14214-3092, USA
SO Journal of Peptide Research (2000), 56(5), 275-282 CODEN: JPERFA; ISSN: 1397-002X
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB Domain 1 of the low-mol.-wt. human salivary mucin, designated MUC7 D1, spans the 51 N-terminal amino acid residues. This domain contains a 15-residue basic histidine-rich subdomain (R3-Q17) which has 53% sequence similarity to ***histatin*** 5 (Hsn-5), a salivary mol. known to exert potent in vitro cidal activity against Candida albicans and many other medically important fungi. The MUC7 D1-15mer and its derivs. have previously been synthesized in our lab. and their candidacidal activities have been found to be inferior to that of Hsn-5. We were therefore intrigued to explore the candidacidal potency of the full-length MUC7 D1 (51-mer). Linear solid-phase synthesis of this domain has been accomplished following std. Fmoc chem. The problems of partial coupling, owing to the peptide chain length, at several stages of the solid-phase step-by-step synthesis were circumvented either by double-coupling techniques or efficient coupling procedures. The MUC7 D1 peptide was purified to homogeneity by conventional reverse-phase HPLC using two columns connected in series. Secondary structure of the purified peptide was assessed by CD (CD) spectroscopy in phosphate buffer and trifluoroethanol and compared to that of MUC7 D1-15mer and Hsn-5. The MUC7 D1 candidacidal activity was assessed against azole-sensitive and azole-resistant C. albicans strains and was found, unlike that of the MUC7 D1-15mer, to be comparable with that of Hsn-5, indicating that in addn. to Hsn-5, MUC7 D1 could provide an

attractive alternative to the classical antifungal agents. The candidacidal potency of MUC7 D1, like that of MUC7 D1-15mer, and of Hsn-5, appears to be largely dependent on peptide charge, irresp. of .alpha.-helical structure.
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 52 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:716574 CAPLUS
DN 134:14963
TI Protein structure and function: ***histatins***
AU Lendenmann, Urs; Oppenheim, Frank G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118-2392, USA
SO Oral Biology at the Turn of the Century: Misconceptions, Truths, Challenges and Prospects, Proceedings of the Conference on the Occasion of the 30th Anniversary of the Founding of the European Research Group of Oral Biology (ERGOB), Interlaken, Switzerland, Aug. 20-23, 1998 (1998), 198-210. Editor(s): Guggenheim, B.; Shapiro, S. Publisher: S. Karger AG, Basel, Switz. CODEN: 69AMID
DT Conference; General Review
LA English
AB A review with 55 refs. on discovery, isolation, characterization and functions of ***histatins*** ; antimicrobial and antifungal activity of salivary ***histatins*** and mechanisms of action in relation to their structure; clin. exploitation of ***histatins*** .
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 53 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:707858 CAPLUS
DN 134:14515
TI Evaluation of the metal binding properties of the histidine-rich antimicrobial peptides ***histatin*** 3 and 5 by electrospray ionization mass spectrometry
AU Brewer, Dyanne; Lajoie, Gilles
CS Guelph-Waterloo Centre for Graduate Work in Chemistry and Biochemistry, Department of Chemistry, University of Waterloo, Waterloo, ON, N2L 3GI, Can.
SO Rapid Communications in Mass Spectrometry (2000), 14(19), 1736-1745 CODEN: RCMSEF; ISSN: 0951-4198
PB John Wiley & Sons Ltd.
DT Journal
LA English
AB Electrospray ionization mass spectrometry (ESI-MS) was used to investigate metal ion interactions with salivary peptides ***histatin*** 3 (H3) and ***histatin*** 5 (H5). Conformational changes of these peptides in the presence of metal ions were studied using CD spectroscopy. H3 and H5 formed high affinity complexes with Cu2+ and Ni2+ and, to a lesser extent, with Zn2+. Both peptides show the potential for multiple binding sites for Cu2+ and Ni2+ and only a single strong binding site for Zn2+. The binding of a third Cu2+ ion to H3 seems to enable the binding of a fourth ion to H3. The binding of a second and third Ni2+ ion to H5 has a similar effect in enabling the binding of a fourth ion. None of the metal ions examd. stabilized a regular secondary structure for either peptide. Subtle changes in overall conformation are seen with the addn. of Cu2+ to both H3 and H5.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 54 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:507633 CAPLUS
DN 133:265568
TI Role of .alpha.-helical conformation of ***histatin*** -5 in candidacidal activity examined by proline variants
AU Situ, H.; Balasubramanian, S. V.; Bobek, L. A.
CS Dep. Oral Biol., Sch. Dental Med., State Univ. New York at Buffalo, Buffalo, NY, 14214, USA
SO Biochimica et Biophysica Acta (2000), 1475(3), 377-382 CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal
LA English
AB Human salivary ***histatin*** -5 (Hsn-5) is a potent in vitro anticandidal agent. The aim of this study was to investigate the importance of .alpha.-helical structure of Hsn-5 for its candidacidal activity. The following three Hsn-5 variants, where one or more functionally nonessential residues were replaced with proline (potent .alpha.-helix breaker), were produced by Escherichia coli expression system: H21P, H19P/H21P (2P), and E16P/H19P/H21P (3P). The activities of purified proteins were detd. by candidacidal assays, and the secondary structures by CD spectroscopy in trifluoroethanol (TFE) that is considered the helix-promoting solvent, and lysophosphatidyl-glycerol (LPG) micelles, the environment that more closely resembles the biol. membranes. The results indicated that 3P variant displayed a candidacidal activity which was similar to that of unaltered Hsn-5 (0P), while 1P and 2P variants showed lower cidal activity. The CD spectra in TFE indicated that 3P variant has less helical characteristics than the 0P, 1P and 2P. These results suggested that the .alpha.-helical content of Hsn-5 proline variants does not correlate with the candidacidal activity. Further, the CD spectral anal. of peptides in LPG micelles indicated the formation of .beta.-turn structures in 0P and 3P variants. In conclusion, 3P variant which exhibited comparable candidacidal activity to 0P contains lower percentage of .alpha.-helical structure than 1P and 2P variants, which exhibited lower candidacidal activity. This suggests .alpha.-helix may not be important for anticandidal activity of Hsn-5.
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 55 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:470702 CAPLUS
DN 133:361133
TI Evaluation of oral health condition in the elderly
AU Terada, Yoko
CS Dep. Removable Prothodontics, Sch. Dent., Tokushima Univ., 3 Kuramoto-cho, Tokushima, 770-8504, Japan
SO Shikoku Shigakkai Zasshi (2000), 13(1), 49-65 CODEN: SSZAED; ISSN: 0914-6091
PB Shikoku Shigakkai
DT Journal
LA Japanese
AB Oral health care for the elderly should be considered as total oral health management, including mastication, speech, swallowing, salivary function and oral hygiene. The purpose of the present study was to evaluate the oral health condition for the oral management. Subjects used were categorized into three groups: healthy young, elderly treated at our dental hospital, and impatients in a geriatric hospital. The pharyngeal microflora was investigated by counting CFUs of total bacteria oral streptococci, staphylococci, Candida spp, and Pseudomonas aeruginosa. Salivary function was investigated by measuring contact angle, concn. of mucin, protein, ***histatins*** , secretory IgA, antibody value to Staphylococcus aureus and Candida albicans. Swallowing duration, tongue force on the palate at swallowing, max. tongue force on the palate, and diadochokinesis of /pa/, /ka/, and /ta/ sounds were measured as evaluation of oral behavior. In the pharyngeal microflora, the no. of total bacteria,

oral streptococci, staphylococci, Candida spp. and Pseudomonas aeruginosa of the elderly groups were higher than those of the young group. And Candida spp. and Pseudomonas aeruginosa were found in the elderly groups only. In salivary function, the concn. of mucin, protein, secretory IgA, antibody value to Staphylococcus aureus and Candida albicans and contact angle of the elderly groups were higher than those of the young group. Concn. of ***histatins*** of the elderly groups was lower than that of the young group. At swallowing of water, swallowing duration was shortened and tongue force at the palate was larger in the elderly group. Maximum tongue force of the elderly was smaller than that of young group. Most valves varied widely in the elderly groups. Therefore, it indicated the difficulty to evaluate the oral health condition of the elderly using age. The present study showed that our evaluation is effective and the oral health condition in the elderly become clear. Further assessment of oral health condition across individuals and groups of elderly people is required for evaluating the oral health condition of each patients and managing appropriate oral health care of the patients.

L3 ANSWER 56 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:436397 CAPLUS
DN 133:347843
TI Effect of donor age on the concentrations of ***histatins*** in human parotid and submandibular/sublingual saliva
AU Johnson, D. A.; Yeh, C.-K.; Dodds, M. W. J.
CS Dental School, Department of Community Dentistry (7917), University of Texas Health Science Center, San Antonio, TX, 78229-3900, USA
SO Archives of Oral Biology (2000), 45(9), 731-740 CODEN: AOBIAR; ISSN: 0003-9969
PB Elsevier Science Ltd.
DT Journal
LA English
AB ***Histatins*** are small proteins of human glandular saliva that have antifungal properties. Recent studies show that oral candidal infections increase with age, suggesting an age-assocd. compromise in oral host defense. Here, the effect of age and of physiol. gland stimulation on the concn. and secretion of salivary ***histatins*** was investigated. Parotid and submandibular/sublingual salivas were collected from six young adults under unstimulated, mech. (chewing) and gustatory (0.025 M and 0.1 M citric acid) stimulation, and the concn. and secretion of ***histatins*** was measured by cationic polyacrylamide gel electrophoresis with subsequent densitometric scanning of the stained gels. With gland stimulation, parotid saliva showed no significant increase in ***histatin*** concn. (.mu.g/mL); however, ***histatin*** secretion (.mu.g/min) increased up to 26-fold ($p<0.005$; ANOVA). Stimulation of submandibular/sublingual saliva resulted in significant increases in both ***histatin*** concn. ($p<0.005$) and secretion ($p<0.0005$). Ageing effects on salivary ***histatins*** were detd. in citric acid (0.1 M)-stimulated parotid and submandibular/sublingual saliva samples collected from 80 individuals (divided into four age groups having approx. equal nos. of males and females: 35-44 yr; 45-54 yr; 55-64 yr and 65-76 yr). None of the patients was taking medications or wore dentures. ANOVA showed no sex differences in ***histatins*** . Regression anal. showed significant age-assocd. decreases for parotid saliva ***histatin*** concn. ($p<0.002$) and secretion ($p<0.002$) as well as for submandibular/sublingual saliva ***histatin*** concn. ($p<0.0001$) and secretion ($p<0.0001$). Both saliva types showed significant ($p<0.0001$) decreases in the ***histatin*** concn. per mg of total protein, suggesting a preferential decrease in salivary ***histatins*** compared to total salivary protein. These results suggest that the salivary ***histatin*** component of the oral host defense system is compromised with increasing age.
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 57 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:381540 CAPLUS
DN 133:219642
TI Simple and rapid purification of ***histatins*** using hydroxyapatite chromatography in denaturalized conditions
AU Kanehira, Takashi; Tani, Hiroshi; Wang, Pao-Li; Ohura, Kiyoshi; Kuboki, Yoshinori
CS Dep. Preventive Dentistry, Hokkaido Univ., Hirakata, 573-1121, Japan
SO Shika Kiso Igakkai Zasshi (2000), 42(2), 160-165 CODEN: SHKKAN; ISSN: 0385-0137
PB Shika Kiso Igakkai
DT Journal
LA English
AB Major ***histatins*** (***histatin*** 1, 3 and 5) from fresh human parotid saliva were sepd. by hydroxyapatite chromatog. in 6 mol/l urea and purified by reversed-phase high performance liq. chromatog. This two-step method enabled us to further study the biochem. and biol. roles of these polypeptides.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 58 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:367584 CAPLUS
DN 133:117326
TI In vitro assessment of antifungal therapeutic potential of salivary ***histatin*** -5, two variants of ***histatin*** -5, and salivary mucin (MUC7) domain 1
AU Situ, Hongsa; Bobek, Libuse A.
CS Department of Oral Biology, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Antimicrobial Agents and Chemotherapy (2000), 44(6), 1485-1493 CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Human salivary ***histatin*** -5 (Hsn-5) is a 24-residue peptide that possesses potent antifungal activity in vitro. The MUC7 gene encodes human salivary low-mol.-wt. mucin (MG2). The candidacidal activity of MUC7 domain 1 (MUC7 D1, the N-terminal 51 amino acid residues of MUC7) in vitro has also been demonstrated. In this study, we have investigated the antifungal therapeutic potential of Hsn-5, its two variants, R12I/K17N and R12I/H21L, and MUC7 D1. First, these peptides were tested for activities against different clin. important fungi. We found them to possess broad-spectrum antifungal activities; specifically, most exhibited excellent in vitro activity against eight clin. important fungal strains tested, including Candida albicans and Candida glabrata and their azole-resistant counterparts and Cryptococcus neoformans and its amphotericin B-resistant counterpart. These findings also suggest that the mechanism of action of both Hsn-5 and MUC7 D1 for these fungi is different from that of amphotericin B or azole antifungal agents. Second, we examd. the stability of these peptides in whole human saliva and human serum. In saliva, the Hsn-5 variants R12I/K17N and R12I/H21L and MUC7 D1 degraded at a lower rate than Hsn-5. In human serum, MUC7 D1 was also more stable than Hsn-5; both peptides were more stable in serum than in saliva. Third, we examd. the cytotoxicity of these peptides using human erythrocytes and two human cell lines (KB and HSG). No (or very low) hemolytic activity was obsd. with any of the four peptides, even at the highest protein concn. tested (200 .mu.M), while amphotericin B

caused 100% hemolysis at only 12.5 .mu.M. The toxic effects of Hsn-5 and MUC7 D1 toward KB and HSG cells were also much lower than that of amphotericin B as measured by trypan blue exclusion. Together, these findings indicate that the investigated peptides possess high antifungal therapeutic potential, in particular for the treatment of drug-resistant fungal strains assocd. with immunocompromised (particularly human immunodeficiency virus-infected) patients. The same peptides could also be used as components of artificial saliva for patients with salivary dysfunction.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 59 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:257642 CAPLUS
DN 133:13891
TI The recombinant N-terminal region of human salivary mucin MG2 (MUC7) contains a binding domain for oral Streptococci and exhibits candidacidal activity
AU Liu, Bing; Rayment, Sean A.; Gyurko, Csilla; Oppenheim, F. G.; Offner, Gwynneth D.; Troxler, Robert F.
CS Department of Periodontology and Oral Biology, Goldman School of Graduate Dentistry, Boston University Medical Center, Boston University School of Medicine, Boston, MA, 02118, USA
SO Biochemical Journal (2000), 345(3), 557-564 CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press Ltd.
DT Journal
LA English
AB MG2 (the MUC7 gene product) is a low-mol.-mass mucin found in human submandibular/sublingual secretions. This mucin is believed to agglutinate a variety of microbes and thus is considered an important component of the non-immune host defense system in the oral cavity. We have shown that MUC7 can bind to cariogenic strains of Streptococcus mutans and that this binding requires a structural determinant in the N-terminal region. In the present study an expression construct, pNMuc7, encoding the N-terminal 144 amino acids of MUC7 was generated, and the recombinant protein rNMUC7 was expressed in Escherichia coli. Purified rNMUC7 was characterized and the binding of this protein to oral bacteria was investigated in an established assay. The results showed that the recombinant protein bound to S. mutans ATCC 25175 and ATCC 33402, and that alkylation of the two cysteine residues (Cys45 and Cys50) resulted in the complete loss of bacterial binding. This suggests that binding of MUC7 to S. mutans occurs between the N-terminal region of the mucin mol. and the bacterial surface, and that this interaction is dependent on a cysteine-contg. domain within this region of MUC7. In addn., the killing activity of rNMUC7 was compared with that of the candidacidal salivary protein ***histatin*** 5 in an established Candida albicans (ATCC 44505) blastoconidia killing assay. It was found that the LD50 values of rNMUC7 and ***histatin*** 5 were comparable, and that the recombinant protein displayed significant killing activity at the physiol. concn. range of MUC7 in whole saliva. This study is the first to show that the N-terminal region of MUC7 contains a structural determinant for bacterial binding and that this region exhibits candidacidal activity.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 60 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:192613 CAPLUS
DN 133:39582
TI Molecular mapping of statherin- and ***histatin*** -binding domains in human salivary mucin MG1 (MUC5B) by the yeast two-hybrid system
AU Iontcheva, I.; Oppenheim, F. G.; Offner, G. D.; Troxler, R. F.
CS Department of Periodontology and Oral Biology, Goldman School of Dental Medicine, Boston, MA, USA
SO Journal of Dental Research (2000), 79(2), 732-739 CODEN: JDREAF; ISSN: 0022-0345
PB International Association for Dental Research
DT Journal
LA English
AB MG1 is a high-mol.-wt. mucin secreted by mucous acinar cells in human submandibular and sublingual glands. We have recently shown that the tracheobronchial mucin MUC5B is a major component of MG1. MUC5B is organized into cysteine-rich N- and C-terminal regions that flank a central tandem-repeat region contg. cysteine-rich subdomains and imperfect 29-residue tandem repeats. In earlier work, we have shown that this mucin selectively forms heterotypic complexes with amylase, proline-rich proteins, statherin, and ***histatins*** in salivary secretions, and the aim of this study was to identify specific binding domains within MUC5B using the yeast two-hybrid system. Interactions of cysteine-rich domains in the tandem-repeat region (Cys1-Cys4) and C-terminal region (Cys8a, Cys8b, Cys8c) of MUC5B with statherin and ***histatins*** were investigated. These studies indicated that ***histatin*** 1 selectively bound to Cys1 and Cys2, whereas statherin and ***histatin*** 1, 3, and 5 selectively bound to Cys8a. Anal. of the primary sequences of the identified binding domains suggests that these domains most probably can fold into globular-like structures in the native mucin. A ProDom blast search revealed that sequences in Cys1, Cys2, and Cys8a exhibit similarity to domains in evolutionarily diverse extracellular proteins known to participate in a wide variety of protein-protein interactions.
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 61 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:138714 CAPLUS
DN 132:345333
TI Antimicrobial activity of synthetic salivary peptides against voice prosthetic microorganisms
AU Elving, G. Jolanda; Van Der Mei, Henny C.; Busscher, Henk J.; Van Nieuw Amerongen, Arie; Veerman, Enno C. I.; Van Weissenbruch, Ranny; Albers, Frans W. J.
CS Departments of Biomedical Engineering and Otorhinolaryngology, University Hospital of Groningen, Groningen, Neth.
SO Laryngoscope (2000), 110(2, Pt. 1), 321-324 CODEN: LARYA8; ISSN: 0023-852X
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB To investigate whether synthetic salivary antimicrobial peptides have an inhibitory effect on the growth of bacteria and yeasts isolated from used silicone rubber voice prostheses. The antimicrobial activities of six synthetic salivary peptides (***histatin*** 5, dhvar1, dhvar4, dhvar5, lactoferrin b 17-30 [LFb 17-30], and cystatin S1-15) at concns. of 2 and 4 mg/mL were detd. against different oropharyngeal yeast (four) and bacterial (eight) strains and against a "total microflora" isolated from explanted voice prostheses using agar diffusion tests. The spectrum of susceptible microorganisms was detd. qual. ***Histatin*** 5 and cystatin S1-15 did not show any antimicrobial activity against the microorganisms involved in this study. Dhvar1 was active against some of the oropharyngeal microorganisms tested, including the yeast strains, but not against Rothia dentocariosa, Staphylococcus aureus, Escherichia coli, and the total microflora. Dhvar4 was active against all microorganisms tested, including the total microflora. Dhvar5

lacked activity against E coli and the total microflora. LFb 17-30 did not inhibit the growth of any of the yeast strains involved and showed only minor activity against some of the bacterial strains. LFb 17-30 slightly inhibited the growth of the total microflora from an explanted prosthesis. The synthetic salivary peptide dhvar4 has a broad antimicrobial activity against all microorganisms that are commonly isolated from explanted voice prostheses, including yeasts. Therewith, it may represent a useful drug, as an alternative for antibiotics and antimycotics employed in various ways to prolong the lifetime of voice prostheses in laryngectomees.
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 62 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:136304 CAPLUS
DN 133:2745
TI Destruction of LPS receptor by Porphyromonas gingivalis protease is prevented by ***histatin*** 5, a specific protease inhibitor
AU Wang, Pao-Li; Sato, Katsuaki; Oido, Mari; Fujii, Takeo; Ohura, Kiyoshi; Kowashi, Yusuke; Tani, Hiroshi; Kuboki, Yoshinori
CS Department of Pharmacology, Osaka Dental University, Hirakata, 573-1121, Japan
SO Journal of Hard Tissue Biology (1999), 8(2), 27-32 CODEN: JHTBFF; ISSN: 1341-7649
PB Society of Hard Tissue Biology
DT Journal
LA English
AB The effect of ***histatin*** 5, a specific inhibitor of an arginine-specific cysteine protease obtained from Porphyromonas gingivalis (Arg-gingipain; P.g. protease), on cultured human gingival epithelial cells (HGEC), was studied. We found that the P.g. lipopolysaccharide (LPS) bound to CD14 on the surface of HGEC and induced the release of interleukin-6 (IL 6). Treating HGEC with P. g. protease destroyed the LPS receptor and reduced IL-6 prodn. to 50% of the control. It was found that addn. of ***histatin*** 5 to the P.g. protease/HGEC system restored IL-6 prodn. by up to 90%. Thus, we conclude that prodn. of IL-6 by HGEC depends on the viability of the LPS receptor. ***Histatin*** 5 prevents the protease-induced inhibition of the HGEC LPS-receptor.
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 63 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:118536 CAPLUS
DN 132:178406
TI Measurement of ***histatins*** in the saliva of healthy humans
AU Wang, Pao-Li; Kanehira, Takashi; Ohura, Kiyoshi; Tani, Hiroshi; Kuboki, Yoshinori
CS Dep. Pharmacol., Osaka Dent. Univ., Sapporo, 573-1121, Japan
SO Shika Kiso Igakkai Zasshi (1999), 41(6), 591-595 CODEN: SHKKAN; ISSN: 0385-0137
PB Shika Kiso Igakkai
DT Journal
LA English
AB Saliva ***histatin*** levels were studied by a competitive ELISA. Levels varied greatly amongst individuals (whole: 0.2-45 .mu.g/mL, parotid: 18.6-82 .mu.g/mL). Parotid levels decreased from 9 a.m. to 7 p.m.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 64 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:117337 CAPLUS
DN 133:41095
TI A study on proteins inhibiting growth of calcium phosphate crystal from human parotid saliva
AU Tada, Tohru
CS Dent. Sch., Okayama Univ., Japan
SO Okayama Shigakkai Zasshi (1999), 18(2), 307-316 CODEN: OSZAE3; ISSN: 0913-3941
PB Okayama Shigakkai
DT Journal
LA Japanese
AB Inhibitory effects on calcium phosphate pptn. were investigated in partially isolated human parotid salivary proteins by an quant. assay method developed for this work. Statherins strongly inhibited calcium phosphate pptn. whereas PRPs and ***histatins*** showed moderate and weak effects.

L3 ANSWER 65 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:69534 CAPLUS
DN 132:205338
TI Candida albicans mutants deficient in respiration are resistant to the small cationic salivary antimicrobial peptide ***histatin*** 5
AU Gyurko, Csilla; Lendenmann, Urs; Troxler, Robert F.; Oppenheim, Frank G.
CS Department of Periodontology and Oral Biology, Boston University Goldman School of Dental Medicine, Boston, MA, 02118-2392, USA
SO Antimicrobial Agents and Chemotherapy (2000), 44(2), 348-354 CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB ***Histatins*** are a group of small cationic peptides in human saliva which are well known for their antibacterial and antifungal activities. In a previous study we demonstrated that ***histatin*** 5 kills both blastoconidia and germ tubes of Candida albicans in a time- and concn.-dependent manner at 37.degree.C, whereas no killing was detected at 4.degree.C. This indicated that killing activity depends on cellular energy. To test ***histatin*** 5 killing activity at lower cellular ATP levels at 37.degree.C, respiratory mutants, or so-called petite mutants, of C. albicans were prepd. These mutants are deficient in respiration due to mutations in mitochondrial DNA. Mutants were initially identified by their small colony size and were further characterized with respect to colony morphol., growth characteristics, respiratory activity, and cytochrome spectra. The killing activity of ***histatin*** 5 at the highest concn. was only 28 to 30% against respiratory mutants, whereas 98% of the wild-type cells were killed. Furthermore, ***histatin*** 5 killing activity was also tested on wild-type cells in the presence of the respiratory inhibitor sodium azide or, alternatively, the uncoupler carbonyl cyanide m-chlorophenylhydrazone. In both cases ***histatin*** 5 killing activity was significantly reduced. Addnl., supernatants and pellets of cells incubated with ***histatin*** 5 in the presence or absence of inhibitors of mitochondrial ATP synthesis were analyzed by sodium dodecyl sulfate gel electrophoresis. It was obsd. that wild-type cells accumulated large amts. of ***histatin*** 5, while wild-type cells treated with inhibitors or petite mutants did not accumulate significant amts. of the peptide. These data showed first that cellular accumulation of ***histatin*** 5 is necessary for killing activity and second that accumulation of ***histatin*** 5 depends on the availability of cellular energy. Therefore, mitochondrial ATP synthesis is required for effective killing activity of ***histatin*** 5.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 66 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:807273 CAPLUS
DN 132:133987
TI Pellicle precursor proteins: Acidic proline-rich proteins, statherin, and ***histatins*** , and their crosslinking reaction by oral transglutaminase
AU Yao, Y.; Lamkin, M. S.; Oppenheim, F. G.
CS Department of Periodontology and Oral Biology, Boston University, Boston, MA, 02118, USA
SO Journal of Dental Research (1999), 78(11), 1696-1703 CODEN: JDREAF; ISSN: 0022-0345
PB International Association for Dental Research
DT Journal
LA English
AB Previous studies have demonstrated that whole saliva and pellicle formed in vitro from oral fluid contain covalently crosslinked salivary proteins. The purpose of this study was to det. which salivary proteins can act as substrates for transglutaminase, an enzyme responsible for the covalent crosslink reaction between a glutamine residue and a lysine residue. Transglutaminase was prepd. from the pellet fraction of human whole saliva. Dansyl cadaverine (N-dansyl-1,5-diaminopentane) was used to study the reactivity of glutamine residues in acidic large and small proline-rich proteins, statherin, and the major ***histatins*** , whereas a glutamine-contg. dansylated peptide was used to study the reactivity of lysine residues in these proteins. Crosslink formation was measured fluorometrically after the addn. of fluorescent probe to the salivary protein substrate and transglutaminase. The covalent attachment of the fluorescent probe to salivary proteins was confirmed by SDS-PAGE. It was found that almost all of the lysines present in the acidic PRPs and statherin, and some of the lysines present in ***histatins*** , could participate in the crosslink reaction. Glutamine reactivity was also obsd., but a max. of only 14% of glutamine residues present in acidic PRPs and statherin participated in the crosslink formation. These results demonstrate that primary pellicle precursor proteins, acidic proline-rich proteins, statherin, and the major ***histatins*** are capable of undergoing crosslink reactions catalyzed by oral transglutaminase. This may enable other proteins in the oral cavity to be incorporated into the acquired enamel pellicle.
RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 67 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:795994 CAPLUS
DN 132:31744
TI Gene probes used for genetic profiling in healthcare screening and planning
IN Roberts, Gareth Wyn
PA Genostic Pharma Ltd., UK
SO PCT Int. Appl., 745 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9964627 A2 19991216 WO 1999-GB1780 19990604 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI GB 1998-12099 A 19980606 GB 1998-13291 A 19980620 GB 1998-13611 A 19980624 GB 1998-13835 A 19980627 GB 1998-14110 A 19980701 GB 1998-14580 A 19980707 GB 1998-15438 A 19980716 GB 1998-15574 A 19980718 GB 1998-15576 A 19980718 GB 1998-16085 A 19980724 GB 1998-16086 A 19980724 GB 1998-16921 A 19980805 GB 1998-17097 A 19980807 GB 1998-17200 A 19980808 GB 1998-17632 A 19980814 GB 1998-17943 A 19980819
AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic" profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L3 ANSWER 68 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:668275 CAPLUS
DN 132:32771
TI Direct Analysis of the Products of Sequential Cleavages of Peptides and Proteins Affinity-Bound to Immobilized Metal Ion Beads by Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry
AU Qian, Xiaohong; Zhou, Wei; Khaledi, Morteza G.; Tomer, Kenneth B.
CS Laboratory of Structure Biology, National Institute of Environmental Health Sciences, National Institutes of Health, Research Triangle Park, NC, 27709, USA
SO Analytical Biochemistry (1999), 274(2), 174-180 CODEN: ANBCA2; ISSN: 0003-2697
PB Academic Press
DT Journal
LA English
AB Consecutive enzymic reactions on analytes affinity-bound to immobilized metal ion beads with subsequent direct anal. of the products by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry have been used for detecting protein synthesis errors occurring at the N-terminus. The usefulness of this method was demonstrated by analyzing two com. available recombinant HIV proteins with affinity tags at the N-terminus,

and ***histatin*** -5, a peptide with multiple histidine residues. The high specificity, sensitivity, and speed of anal. make this method esp. useful in obtaining N-terminal sequencing information of histidine-tagged recombinant proteins. (c) 1999 Academic Press.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 69 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:593998 CAPLUS
DN 131:320123
TI Synergistic actions of nisin, sublethal ultrahigh pressure, and reduced temperature on bacteria and yeast
AU Ter Steeg, Pieter F.; Hellemons, Johan C.; Kok, Anja E.
CS Microbiology and Preservation, Unilever Research Vlaardingen, Vlaardingen, 3130 AC, Neth.
SO Applied and Environmental Microbiology (1999), 65(9), 4148-4154 CODEN: AEMIDF; ISSN: 0099-2240
PB American Society for Microbiology
DT Journal
LA English
AB Nisin in combination with ultrahigh-pressure treatment (UHP) showed strong synergistic effects against Lactobacillus plantarum and Escherichia coli at reduced temps. (<15.degree.). The strongest inactivation effects were obsd. when nisin was present during pressure treatment and in the recovery medium. Elimination (>6-log redns.) of L. plantarum was achieved at 10.degree. with synergistic combinations of 0.5 .mu.g nisin/mL at 150 MPa and 0.1 .mu.g nisin/mL at 200 MPa for 10 min. Additive effects of nisin and UHP accounted for only 1.2- and 3.7-log redns., resp. Elimination was also achieved for E. coli at 10.degree. with nisin present at 2 .mu.g/mL, and 10 min of pressure at 200 MPa, whereas the additive effect accounted for only 2.6-log redns. Slight effects were obsd. even against the yeast Saccharomyces cerevisiae with nisin present at 5 .mu.g/mL and with 200 MPa of pressure. Combining nisin, UHP, and lowered temp. may allow considerable redn. in time and/or pressure of UHP treatments. Kill can be complete without the frequently encountered survival tails in UHP processing. The slightly enhanced synergistic kill with UHP at reduced temps. was also obsd. for other antimicrobials, the synthetic peptides MB21 and ***histatin*** 5. The postulated mode of action was that the reduced temp. and the binding of peptides to the membrane increased the efficacy of UHP treatment. The increases in fatty acid satn. or diphosphatidylglycerol content and the lysylphosphatidyl content of the cytoplasm membrane of L. plantarum were correlated with increased susceptibility to UHP and nisin, resp.
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 70 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:585883 CAPLUS
DN 131:297512
TI ***Histatin*** 3-mediated killing of Candida albicans: effect of extracellular salt concentration on binding and internalization
AU Xu, Yanying; Ambudkar, Indu; Yamagishi, Hisako; Swaim, William; Walsh, Thomas J.; O'Connell, Brian C.
CS Gene Therapy and Therapeutics Branch, Bethesda, MD, 20892, USA
SO Antimicrobial Agents and Chemotherapy (1999), 43(9), 2256-2262 CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB Human saliva contains histidine-rich proteins, ***histatins*** , which have antifungal activity in vitro. The mechanism by which ***histatins*** are able to kill Candida albicans may have clin. significance but is currently unknown. Using radiolabeled ***histatin*** 3, we show that the protein binds to C. albicans spheroplasts in a manner that is dependent on time and concn. Binding to the spheroplasts was saturable and could be competed with unlabeled ***histatin*** 3. A single ***histatin*** 3 binding site with a Kd = 5.1 .mu.M was detected. ***Histatin*** 3 binding resulted in potassium and magnesium efflux, predominantly within the first 30 min of incubation. Studies with fluorescent ***histatin*** 3 demonstrate that the protein is internalized by C. albicans and that translocation of ***histatin*** inside the cell is closely assocd. with cell death. ***Histatin*** binding, internalization, and cell death are accelerated in low-ionic-strength conditions. Indeed, a low extracellular salt concn. was essential for cell death to occur, even when ***histatin*** 3 was already bound to the cell. The interaction of ***histatin*** 3 with C. albicans, and subsequent cell death, is inhibited at low temp. These results demonstrate that the candidacidal activity of ***histatin*** 3 is not due exclusively to binding at the cell surface but also involves subsequent interactions with the cell.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 71 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:441598 CAPLUS
DN 131:196899
TI Salivary ***histatin*** 5 induces non-lytic release of ATP from Candida albicans leading to cell death
AU Koshlukova, Svetlana E.; Lloyd, Tracy L.; Araujo, Marcelo W. B.; Edgerton, Mira
CS Departments of Oral Biology and Restorative Dentistry, School of Dental Medicine, State University of New York at Buffalo, New York, 14214, USA
SO Journal of Biological Chemistry (1999), 274(27), 18872-18879 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Salivary ***histatins*** are potent in vitro antifungal proteins and have promise as therapeutic agents against oral candidiasis. We performed pharmacol. studies directed at understanding the biochem. basis of Hst 5 candidacidal activity. Three inhibitors of mitochondrial metab.: carbonyl cyanide p-chlorophenylhydrazone, dinitrophenol, and azide inhibited Hst 5 killing of Candida albicans, while not inhibiting cellular ATP prodn. In contrast, Hst 5 caused a drastic redn. of C. albicans intracellular ATP content, which was a result of an efflux of ATP. Carbonyl cyanide p-chlorophenylhydrazone, dinitrophenol, and azide inhibited Hst 5-induced ATP efflux, thus establishing a correlation between ATP release and cell killing. Furthermore, C. albicans cells were respiring and had polarized membranes at least 80 min after ATP release, thus implying a non-lytic exit of cellular ATP in response to Hst 5. Based on evidence that transmembrane ATP efflux can occur in the absence of cytolysis through a channel-like pathway and that released ATP can act as a cytotoxic mediator by binding to membrane purinergic receptors, we evaluated whether extracellular ATP released by Hst 5 may have further functional role in cell killing. Consistent with this hypothesis, purinergic agonists BzATP and adenosine 5'O-(thiotriphosphate) induced loss of C. albicans cell viability and purinergic antagonists prevented Hst 5 killing.
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 72 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:410996 CAPLUS

DN 131:213090
TI Zn2+ ions selectively induce antimicrobial salivary peptide ***histatin*** -5 to fuse negatively charged vesicles. Identification and characterization of a zinc-binding motif present in the functional domain
AU Melino, Sonia; Rufini, Stefano; Sette, Marco; Morero, Roberto; Grottesi, Alessandro; Paci, Maurizio; Petruzzelli, Raffaele
CS Dipartimento di Scienze Biomediche, Universita di Chieti G. D'Annunzio, Chieti, 66100, Italy
SO Biochemistry (1999), 38(30), 9626-9633 CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
AB The salivary antimicrobial peptide ***histatin*** -5 is able to aggregate and fuse neg. charged small unilamellar vesicles, and this fusogenic activity is selectively induced by the presence of zinc ions. CD spectroscopy shows that ***histatin*** -5, in the presence of neg. charged vesicles and zinc ions, undergoes a conformational change leading to the stabilization of an .alpha.-helical secondary structure. The authors attribute the specific action of the zinc ions to the presence of a consensus sequence, HEXXH, located in the C-terminal functional domain of ***histatin*** -5, a recognized zinc-binding motif in many proteins. Two-dimensional proton NMR spectroscopy of ***histatin*** -5 in a trifluoroethanol/water mixt. (a membrane mimetic environment) has been performed and the results analyzed by distance geometry and restrained mol. dynamics simulations. The authors' results reveal that the peptide chain, including the Zn-binding consensus sequence corresponding to residues 15-19, is in a helicoidal conformation. Comparison of the chem. shifts of the individual amino acids in ***histatin*** -5 with those recently reported in other solvents indicates that trifluoroethanol/water has a structuring capability somewhere between water and DMSO. The mechanism of action of this antimicrobial peptide is discussed on the basis of its structural characteristics with particular attention to the Zn-binding motif.
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 73 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:393960 CAPLUS
DN 131:39718
TI Antifungal and antibacterial ***histatin*** -based peptides
IN Oppenheim, Frank G.; Xu, Tao; Roberts, F. Donald; Spacciapoli, Peter; Friden, Phillip M.
PA Periodontix, Inc., USA; Trustees of Boston University
SO U.S., 35 pp., Cont.-in-part of U.S. 5,631,228. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI US 5912230 A 19990615 US 1998-973559 19980311 US 5486503 A 19960123 US 1994-287717 19940809 US 5631228 A 19970520 US 1995-481888 19950607 WO 9640768 A2 19961219 WO 1996-US9374 19960607 WO 9640768 A3 19970306 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA PRAI US 1991-786571 B1 19911101 US 1993-145030 B1 19931028 US 1994-287717 A2 19940809 US 1995-481888 A2 19950607 WO 1996-US9374 W 19960607
AB ***Histatin*** -based peptides representing defined portions of the amino acid sequences of naturally occurring human ***histatins*** , and methods for treatment of fungal or bacterial infection, are described. The ***histatin*** -based peptides represent the active anti-fungal and anti-bacterial region of naturally occurring human ***histatins*** .
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 74 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:393705 CAPLUS
DN 131:211488
TI The effects of ***histatin*** -derived basic antimicrobial peptides on oral biofilms
AU Helmerhorst, E. J.; Hodgson, R.; Van't Hof, W.; Veerman, E. C. I.; Allison, C.; Amerongen, A. v. Nieuw
CS Academic Centre for Dentistry (ACTA), Vrije Universiteit, Department of Oral Biochemistry, Amsterdam, 1081 BT, Neth.
SO Journal of Dental Research (1999), 78(6), 1245-1250 CODEN: JDREAF; ISSN: 0022-0345
PB International Association for Dental Research
DT Journal
LA English
AB Susceptibility of bacteria to antimicrobial agents is strongly reduced by the formation of complex biofilms. We investigated whether synthetic ***histatin*** analogs with broad-spectrum antibacterial activity in vitro were also active against these complex mixts. of bacteria, as present in saliva and plaque. In a simplified model system for dental plaque, hydroxylapatite disks were placed in a continuous culture system comprised of Streptococcus mutans, S. sanguis, S. salivarius, Actinomyces naeslundii, Veillonella parvula, Fusobacterium nucleatum, and Prevotella intermedia. Ex situ treatment of the biofilms formed on these disks with 100 .mu.g/mL of peptide dhvar4 significantly reduced facultative anaerobic, total anaerobic, and obligate anaerobic Gram-neg. counts with 0.8, 0.5, and 0.5 log units, resp. Ex vivo treatment of salivary bacteria gave redns. of 0.4, 0.7, and 1.5 log units, resp. For ex vivo treatment of plaque bacteria, redns. of 0.4, 0.4, and 1.4 log units, resp., were found. In both saliva and plaque samples, obligate anaerobic Gram-neg. bacteria were significantly more susceptible to dhvar4 than facultatively anaerobic or anaerobic bacteria as a whole ($p = 0.013$ and $p = 0.018$, for salivary bacteria, and $p = 0.021$ and $p = 0.020$ for plaque bacteria, resp.). Although the oral bacteria are protected by biofilm formation, the synthetic ***histatin*** analog caused a significant redn. of viable counts in a model for oral biofilm as well as in isolated oral biofilms.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 75 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:376062 CAPLUS
DN 131:174970
TI Evaluation of the use of xanthan as vehicle for cationic antifungal peptides
AU Ruissen, A. L. A.; van der Reijden, W. A.; van't Hof, W.; Veerman, E. C. I.; Nieuw Amerongen, A. V.
CS Department of Oral Biochemistry, Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam, 1081 BT, Neth.
SO Journal of Controlled Release (1999), 60(1), 49-56 CODEN: JCREEC; ISSN: 0168-3659
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB Oral candidiasis frequently occurs in individuals with dry mouth syndrome (xerostomia), in immunocompromised patients and in denture wearers. The aim of this study was to develop a formulation which will prolong the retention time of antimicrobial agents at the site of application. The activity against Candida

albicans of a synthetic cationic peptide dhvar 1, based on the human fungicidal salivary peptide ***histatin*** 5, was tested either in a mixt. with the bioadhesive polymer xanthan, or after covalent coupling to this polymer. The presence of xanthan resulted in an increase of the LC50 value of the peptide from 2.6 (S.D.=0.6) to 5.8 (S.D.=4.0). Covalent coupling caused an addnl. increase of the LC50 value to 18.4 (S.D.=6.7). Coupling caused a redn. of the viscosity and elasticity of the xanthan soln. related to the applied concn. of the coupling agent. Incubation of the peptide with clarified human whole saliva resulted in proteolytic degrdn. of the peptide. In the presence of xanthan the degrdn. occurred more slowly. It was concluded that xanthan is an appropriate vehicle for antimicrobial peptides in a retention increasing formulation.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 76 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:293162 CAPLUS
DN 131:126859
TI Candidacidal activity prompted by N-terminus ***histatin*** -like domain of human salivary mucin (MUC7)
AU Gururaja, Tarikere L.; Levine, Joseph H.; Tran, Duy T.; Naganagowda, Gowda A.; Ramalingam, Kalaiyarasi; Ramasubbu, Narayanan; Levine, Michael J.
CS Department of Oral Biology and Dental Research Institute, State University of New York at Buffalo, Buffalo, NY, USA
SO Biochimica et Biophysica Acta (1999), 1431(1), 107-119 CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier Science B.V.
DT Journal
LA English
AB Histidine-rich peptides (***histatins*** , Hsn) in saliva are thought to provide a non-immune defense against Candida albicans. Sequence homol. search of the human salivary mucin, MUC7, against ***histatins*** revealed a domain at the N-terminus (R3-Q17) having 53% identity to Hsn-5. To det. its candidacidal activity, this 15 residue basic histidine-rich domain of MUC7 (I) was prepd. by solid-phase Fmoc chem. Various N- and C-terminal protected derivs. of I were also synthesized to correlate the effect of peptide overall charge in exhibiting cidal potency. Candidacidal activity measurement of I and its variants showed considerable ED50 values (effective dosage required to kill 50% of Candida cells), albeit greater than Hsn-5 (ED50 .apprx.4-6 .mu.M). Of the various analogs tested, N-terminal free acid (I, ED50 .apprx.40 .mu.M) and amide (V, ED50.apprx.16 .mu.M) exhibited appreciable candidacidal activities suggesting the possible role of peptide net charge in cidal action. Blocking of N-terminus with a bulky octanoyl group showed only marginal effect on the cidal activity of I or V, indicating that hydrophobicity of these synthetic constructs may not be important for exerting such activities. Membrane-induced conformational transition from random coil to helical structures of all the test peptides implied their tendency to adapt order structures at the lipid-membrane interface similar to that of Hsn-5. However, comparison of propensity for helical structure formation vs. ED50 indicated that cidal potency of MUC7 Hsn-like peptides depends largely on electrostatic interactions irresp. of secondary structural elements. Delineation of soln. structure of the most active peptide (V) by 2D-NMR revealed essentially a non-structured conformation in aq. medium, which further supported the fact that the peptide helical structure may not be a prerequisite for posing candidacidal activity. The formation of smaller truncated peptides and/or Hsn-like fragments on proteolytic degrdn. of intact MUC7 in the presence of oral flora provided indirect evidence that mucin could serve as a backup candidacidal agent to salivary Hsn.
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 77 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:278105 CAPLUS
DN 131:72852
TI Interaction of Tannin with Human Salivary ***Histatins***
AU Naurato, Nicholas; Wong, Peggy; Lu, Ying; Wroblewski, Karol; Bennick, Anders
CS Faculty of Dentistry and Department of Biochemistry, University of Toronto, Toronto, ON, M5S 1A8, Can.
SO Journal of Agricultural and Food Chemistry (1999), 47(6), 2229-2234 CODEN: JAFCAU; ISSN: 0021-8561
PB American Chemical Society
DT Journal
LA English
AB The ability of all major human salivary ***histatins*** to ppt. condensed tannin was demonstrated, and it was found that ***histatins*** 3 and 5 share the same condensed tannin-binding region but less tannin bound to ***histatin*** 1. The condensed tannin-binding region of ***histatin*** 5 includes both the N- and the C-terminal parts, although more tannin binding occurs in the C-terminal region. Epigallocatechin gallate (EGCG) showed similar binding characteristics as condensed tannin, but much less EGCG was pptd. Pentagalloyl glucose (PGG) was pptd. equally well by ***histatins*** 1, 3, and 5 and bound equally well to the N- and C-terminal regions of ***histatin*** 5. In contrast to condensed tannin, cleaving ***histatin*** 5 into N- and C-terminal fragments increased their ability to ppt. PGG. Together, these results show a no. of differences in the nature of interaction of ***histatins*** with condensed tannin, EGCG, and PGG. Most of the condensed tannin-protein complexes remained insol. under conditions similar to those in the stomach and the small intestine, suggesting that ***histatins*** may act as a defense against dietary tannin in humans.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 78 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:262855 CAPLUS
DN 131:97008
TI A critical comparison of the hemolytic and fungicidal activities of cationic antimicrobial peptides
AU Helmerhorst, Eva J.; Reijnders, Ingrid M.; van 't Hof, Wim; Veerman, Enno C. I.; Nieuw Amerongen, Arie V.
CS Department of Oral Biochemistry, Academic Centre for Dentistry Amsterdam (ACTA), Vrije Universiteit, Van der Boechorststraat 7, Amsterdam, 1081 BT, Neth.
SO FEBS Letters (1999), 449(2,3), 105-110 CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
AB The hemolytic and fungicidal activity of a no. of cationic antimicrobial peptides was investigated. ***Histatins*** and magainins were inactive against human erythrocytes and Candida albicans cells in phosphate buffered saline, but displayed strong activity against both cell types when tested in 1 mM potassium phosphate buffer supplemented with 287 mM glucose. The HC50/IC50 ratio, indicative of the therapeutic index, was about 30 for all peptides tested. PGLa was most hemolytic (HC50=0.6 .mu.M) and had the lowest therapeutic index (HC50/IC50=0.5). Susceptibility to hemolysis was shown to increase with storage duration of the erythrocytes and also significant differences were found between blood collected from different individuals. In this report, a sensitive assay is proposed for the testing of the

hemolytic activities of cationic peptides. This assay detects subtle differences between peptides and allows the comparison between the hemolytic and fungicidal potency of cationic peptides.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 79 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:245232 CAPLUS
DN 131:71595
TI Amino acid sequences of arginine peptides from human whole saliva
AU Sato, Noriko; Inoue, Michi; Sanada, Kazuo
CS Department of Biochemistry, School of Dentistry at Tokyo, The Nippon Dental University, Tokyo, 102-8159, Japan
SO Shika Kiso Igakkai Zasshi (1999), 41(1), 21-26 CODEN: SHKKAN; ISSN: 0385-0137
PB Shika Kiso Igakkai
DT Journal
LA Japanese
AB We attempted to sep. several arginine oligopeptides from human whole saliva and to confirm the presence of sialin (GGKR). The methanol sol. fraction of whole saliva was subjected to gel filtration on a Bio-Gel P-6 column. Fraction III (substances estd. to be less than 10,000 Da) was ultrafiltered to remove the fraction greater than 5,000 Da, and purified by affinity chromatog. on an anhydrotrypsin agarose column. Fourteen peptides were obtained from the fraction adsorbed on affinity column with further purifn. by high-performance liq. chromatog. (RP-HPLC). The amino acid anal. indicated that ten oligopeptides purified were histidine-rich arginine peptides. Sequencing of five major peptides revealed that these low mol. wt. arginine peptides were derived from ***histatin*** by proteolysis. The mol. wt. of the major arginine peptides ranged from 800 to 1,600 Da. Sialin was not detected in this study.

L3 ANSWER 80 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:208580 CAPLUS
DN 130:232464
TI Antifungal and antibacterial D-amino acid ***histatin*** -based peptides
IN Oppenheim, Frank G.; Xu, Tao; Roberts, F. Donald; Spacciapoli, Peter; Friden, Phillip M.
PA Periodontix, Inc., USA; Trustees of Boston University
SO U.S., 34 pp., Cont.-in-part of U.S. 5,631,228. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI US 5885965 A 19990323 US 1998-973563 19980312 US 5486503 A 19960123 US 1994-287717 19940809 US 5646119 A 19970708 US 1995-485273 19950607 WO 9640770 A2 19961219 WO 1996-US9962 19960607 WO 9640770 A3 19970206 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA
PRAI US 1991-786571 B1 19911101 US 1993-145030 B1 19931028 US 1994-287717 A2 19940809 US 1995-485273 A2 19950607 WO 1996-US9962 W 19960607
AB D-Amino acid ***histatins*** and ***histatin*** -based peptides and methods for treatment of fungal or bacterial infection are described. These D-amino acid ***histatins*** and ***histatin*** -based peptides are longer-acting antifungal or antibacterial agents than their L-enantiomeric analogs.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 81 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:191911 CAPLUS
DN 130:349611
TI The cellular target of ***histatin*** 5 on Candida albicans is the energized mitochondrion
AU Helmerhorst, Eva J.; Breeuwer, Pieter; Van't Hof, Wim; Walgreen-Weteringst, Els; Oomen, Lauran C. J. M.; Veermant, Enno C. I.; Nieuw Amerongen, Arie V.; Abee, Tjakko
CS Academic Centre for Dentistry, Department of Oral Biochemistry, Vrije Universiteit, Amsterdam, 1081 BT, Neth.
SO Journal of Biological Chemistry (1999), 274(11), 7286-7291 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB ***Histatin*** 5 is a human basic salivary peptide with strong fungicidal properties in vitro. To elucidate the mechanism of action, the effect of ***histatin*** 5 on the viability of Candida albicans cells was studied in relation to its membrane perturbing properties. It was found that both the killing activity and the membrane perturbing activity, studied by the influx of a DNA-specific marker propidium iodide, were inhibited by high salt conditions and by metabolic inhibitors, like sodium azide. In addn., exposure to ***histatin*** 5 resulted in a loss of the mitochondrial transmembrane potential in situ, measured by the release of the potential-dependent distributional probe rhodamine 123. Localization studies using tetramethylrhodamine isothiocyanate-labeled ***histatin*** 5 or fluorescein isothiocyanate-labeled ***histatin*** 5 showed a granular intracellular distribution of the peptide, which co-localized with mitotracker orange, a permeant mitochondria-specific probe. Like the biol. effects, uptake of labeled ***histatin*** 5 was inhibited by mitochondrial inhibitors and high salt conditions. Our data indicate that ***histatin*** 5 is internalized and targets to the energized mitochondrion.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 82 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:159301 CAPLUS
DN 130:322846
TI Amphotericin B- and fluconazole-resistant Candida spp., Aspergillus fumigatus, and other newly emerging pathogenic fungi are susceptible to basic antifungal peptides
AU Helmerhorst, Eva J.; Reijnders, Ingrid M.; Van 't Hof, Wim; Simoons-Smit, Ina; Veerman, Enno C. I.; Nieuw Amerongen, Arie V.
CS Academic Centre for Dentistry (ACTA), Department of Oral Biochemistry, Vrije Universiteit, Amsterdam, 1081 BT, Neth.
SO Antimicrobial Agents and Chemotherapy (1999), 43(3), 702-704 CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB The present study shows that a no. of basic antifungal peptides, including human salivary ***histatin*** 5, a designed ***histatin*** analog designated dhvar4, and a peptide from frog skin, PGLa, are active against amphotericin B-resistant Candida albicans, Candida krusei, and Aspergillus fumigatus strains and against a fluconazole-resistant Candida glabrata isolate.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 83 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:148931 CAPLUS
DN 131:13348
TI Construction and characterization of human salivary ***histatin*** -5 multimers
AU Situ, H.; Tsai, H.; Bobek, L. A.
CS Department of Oral Biology, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Journal of Dental Research (1999), 78(2), 690-698 CODEN: JDREAF; ISSN: 0022-0345
PB International Association for Dental Research
DT Journal
LA English
AB Human salivary ***histatin*** -5 (Hsn-5), a 24-amino acid polypeptide, is a potent candidacidal mol. In this study, we have explored the following two hypotheses: more potent Hsn mols. may be achieved by duplication of the functional domain of Hsn-5 (C16, residues 9-24 of Hsn-5), and Hsn may act like other cationic peptides which aggregate and form channels across the target membrane. A PCR-based gene splicing by overlap extension (SOE) method was used to construct the DNA fragments encoding the following fusion mols.: Hsn-5-Hsn-5, Hsn-5-C16, and C16-C16. These constructs were expressed in E. coli, the proteins produced were purified, and their anticandidal activities as well as secondary structures were detd. Contrary to our hypotheses, results showed that none of the multimers possessed increased candidacidal activity. Specifically, C16-C16 and Hsn-5-C16 displayed candidacidal activity comparable with that of Hsn-5, while Hsn-5-Hsn-5 possessed significantly decreased candidacidal activity, yet all mols. retained an .alpha.-helical structure in a hydrophobic environment. Addnl., the CD data showed that Hsn-5 in an .alpha.-helical conformation does not aggregate in a hydrophobic environment, not even at 14- to 18-fold its physiol. concn. Our results suggest that the development of enhanced Hsn-5 mols. may not be achieved by duplication of its functional domain, and that Hsns may not act like other antimicrobial cationic peptides which aggregate and form channels across the target membrane.
RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 84 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:132402 CAPLUS
DN 130:295175
TI Antimicrobial peptides in mammalian and insect host defense
AU Lehrer, Robert I.; Ganz, Tomas
CS Department of Medicine, The Molecular Biology Institute, UCLA School of Medicine, Los Angeles, CA, 90095, USA
SO Current Opinion in Immunology (1999), 11(1), 23-27 CODEN: COPIEL; ISSN: 0952-7915
PB Current Biology Publications
DT Journal; General Review
LA English
AB A review with 54 refs. During the past year, addnl. insights into systems that regulate antimicrobial peptide prodn. in Drosophila were reported. Granulysin, a peptide stored in the cytoplasmic granules of human natural killer cells and cytolytic T cells, was shown to kill Mycobacterium tuberculosis. More data implicating antimicrobial peptides in the pathogenesis of bronchopulmonary infections in cystic fibrosis appeared. Studies that examd. the potential contributions of antimicrobial peptides to regional innate immunity gained in prominence. Efforts to design peptide analogs to prevent or treat infections continued. Topics discussed include defensins, cathelicidins, protegrins, ***histatins*** , granulysin, secretory leukoprotease inhibitor, probiotics, and Drosophila antimicrobial peptides.
RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 85 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:51280 CAPLUS
DN 130:206476
TI NMR studies of the antimicrobial salivary peptides ***histatin*** 3 and ***histatin*** 5 in aqueous and nonaqueous solutions
AU Brewer, Dyanne; Hunter, Howard; Lajoie, Gilles
CS Guelph-Waterloo Centre for Graduate Work Chemistry and Biochemistry, Department of Chemistry, University of Waterloo, Waterloo, ON, N2L 3G1, Can.
SO Biochemistry and Cell Biology (1998), 76(2/3), 247-256 CODEN: BCBIEQ; ISSN: 0829-8211
PB National Research Council of Canada
DT Journal
LA English
AB Conformational studies of the salivary peptides ***histatin*** 3 (H3) and ***histatin*** 5 (H5) were performed by NMR and CD in aq. and nonaq. solns. ***Histatin*** 5 has no defined structure in H2O but adopts a more helical conformation in DMSO and aq. trifluoroethanol. This is in agreement with the CD anal., which shows no secondary structure in H2O but increasing helical content in the presence of trifluoroethanol. CD anal. shows that H3 has less propensity to form a helical structure than H5 in similar conditions. The NMR anal. of H3 in H2O at pH 7.4 reveals that its conformational mobility is less than that of H5 as indicated by the observation of backbone cross peaks .alpha.N (i, i + 1) and NN (i, i + 1) and the slow exchanging amide protons in the C-terminus. However, H3 remains essentially unordered as suggested by the lack of longer range nuclear Overhauser effects (NOEs) in the NOESY spectrum. H3 becomes much more ordered in a mixt. of 50:50 H2O - DMSO as indicated by the numerous NOEs, including several side chain to side chain and side chain to backbone connectivities. Our data suggest that in these conditions H3 contains a turn in the region of K13 to K17 and possibly a 310 helix at the C-terminus. This study demonstrates that H3 and H5 are both conformationally mobile and that each adopts different types of conformations in aq. and nonaq. solns.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 86 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:770974 CAPLUS
DN 130:150655
TI Human salivary ***histatins*** : Promising anti-fungal therapeutic agents
AU Tsai, H.; Bobek, L. A.
CS Department of Oral Biology, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Critical Reviews in Oral Biology & Medicine (1998), 9(4), 480-497 CODEN: CROMEF; ISSN: 1045-4411
PB International and American Associations for Dental Research
DT Journal; General Review
LA English
AB A review with 110 refs. ***Histatins*** constitute a group of small, cationic multifunctional proteins present in the saliva of human and some nonhuman primates. The most significant function of ***histatins*** may be their anti-fungal activity against Candida albicans and Cryptococcus neoformans. ***Histatins*** have been extensively studied at both the protein and gene levels. The structure-function relationship of ***histatins*** with respect to their candidacidal activity has also been studied by means of recombinant ***histatin*** variants, as well as by chem. synthesized ***histatin*** fragments. The mechanism of ***histatins*** ' action on

Candida albicans is not clear, but it appears to be different from that of azole-based anti-fungal drugs which interrupt ergosterol synthesis. During the past 20 yr, fungal infections have become more prevalent as a result of the emergence of AIDS, as well as, paradoxically, modern medical advances. The toxicity of current anti-fungal medicine, the emergence of drug-resistant strains, and the availability of only a few types of anti-fungal agents are the major disadvantages of current anti-fungal therapy. Therefore, the importance of the search for new, broad-spectrum anti-fungals with little or no toxicity cannot be overemphasized. The following properties make ***histatins*** promising anti-fungal therapeutic agents: (1) They have little or no toxicity; (2) they possess high cidal activities against azole-resistant fungal species and most of the fungal species tested; and (3) their candidacidal activity is similar to that of azole-based antifungals. Current research efforts focus on the development of improved ***histatins*** with enhanced cidal activity and stability, and of suitable and effective ***histatin*** delivery systems. These and other approaches may help to outpace the growing list of drug-resistant and opportunistic fungi causing life-threatening, disseminating diseases. The ***histatins*** with improved protective properties may also be used as components of artificial saliva for patients with salivary dysfunction.
RE.CNT 118 THERE ARE 118 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 87 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:628726 CAPLUS
DN 130:22069
TI ***Histatin*** 5 is a substrate and not an inhibitor of the Arg- and Lys-specific proteinases of Porphyromonas gingivalis
AU O'Brien-Simpson, Neil M.; Dashper, Stuart G.; Reynolds, Eric C.
CS Biochemistry and Molecular Biology Unit, School of Dental Science, The University of Melbourne, Melbourne, 3000, Australia
SO Biochemical and Biophysical Research Communications (1998), 250(2), 474-478 CODEN: BBRCA9; ISSN: 0006-291X
PB Academic Press
DT Journal
LA English
AB The salivary peptide ***histatin*** 5 has been reported to be an inhibitor of the Arg- and Lys-specific proteinases of Porphyromonas gingivalis, an oral pathogen assocd. with periodontitis. In this study a purified P. gingivalis proteinase prepn. consisting of a complex of the Arg- and Lys-specific proteinases and adhesins was assayed using chromogenic substrates in the presence of ***histatin*** 5. ***Histatin*** 5 produced a concn.-dependent decrease in the initial rate of hydrolysis of the chromogenic substrates by both proteinases. However, pre-incubation of ***histatin*** 5 with the purified proteinase prepn. or a P. gingivalis cell sonicate for 10 min prior to assay with the chromogenic substrates showed that under these conditions the salivary peptide did not decrease the initial rate of chromogen release. Mass spectrometric anal. revealed rapid degrdn. of ***histatin*** 5 at all four lysyl and all three arginyl residues by the P. gingivalis proteinases. This study demonstrates that ***histatin*** 5 is a substrate for the P. gingivalis extracellular Arg- and Lys-specific cysteine proteinases and not an inhibitor. (c) 1998 Academic Press.
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 88 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:618824 CAPLUS
DN 129:229692
TI Photosensitizer conjugates for pathogen targeting
IN Hasan, Tayyaba; Hamblin, Michael R.; Soukos, Nikos
PA The General Hospital Corporation, USA
SO PCT Int. Appl., 74 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9839011 A1 19980911 WO 1998-US4001 19980227 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG US 6462070 B1 20021008 US 1997-812606 19970306 AU 9866767 A1 19980922 AU 1998-66767 19980227 AU 737574 B2 20010823 EP 1017397 A1 20000712 EP 1998-908829 19980227 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI JP 2001513819 T2 20010904 JP 1998-538642 19980227 US 2002183245 A1 20021205 US 2002-143593 20020509
PRAI US 1997-812606 A2 19970306 WO 1998-US4001 W 19980227
AB Conjugate mols. which include photosensitizer compns. conjugated to non-antibody non-affinity pair targeting moieties and methods of making and using such conjugates are described. The non-pair member moiety includes a bacterial, fungal, or animal (e.g. mammalian or human) small antimicrobial peptide: ***histatin*** , defensin, cecropin, magainin, gram-pos. bacteriocin, and antibiotic peptide, and the photosensitizer is a porphyrin or deriv. Thus, polylysin-chlorin e6 conjugates, ***histatin*** -chlorin e6 conjugates, and ***histatin*** - polylysine-chlorin e6 conjugates of varying charges were synthesized and tested for uptake by Porphyromonas gingivalis and phototoxicity of these conjugates for killing bacteria while sparing mammalian cells.
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 89 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:541378 CAPLUS
DN 129:244098
TI Candidacidal activity of salivary ***histatins*** . Identification of a ***histatin*** 5-binding protein on Candida albicans
AU Edgerton, Mira; Koshlukova, Svetlana E.; Lo, Thomas E.; Chrzan, Brian G.; Straubinger, Robert M.; Raj, Periathamby A.
CS Department of Oral Biology, School of Dental Medicine, State University of New York, Buffalo, NY, 14214, USA
SO Journal of Biological Chemistry (1998), 273(32), 20438-20447 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB Candida albicans is the predominant species of yeast isolated from patients with oral candidiasis, which is frequently a symptom of human immunodeficiency virus infection and is a criterion for staging and progression of AIDS. Salivary ***histatins*** (Hsts) are potent in vitro antifungal agents and have great promise as therapeutic agents in humans with oral candidiasis. The mol. mechanisms by which Hsts kill yeast cells are not known. We report here, that unlike other antimicrobial proteins, Hsts do not display lytic activities to lipid membranes, measured by release and dequenching of the fluorescent dye calcein. Anal. of the magnitude and time course of Hst-induced calcein release from C. albicans cells further showed that loss of cell integrity was a secondary effect following cell death, rather

than the result of primary disruption of the yeast cell membrane. 125I-Hst 5 binding studies indicated that C. albicans expressed a class of saturable binding sites (KD = 1 .mu.M), numbering 8.6 .times. 105 sites/cell. Both Hst 3 and Hst 4 competed for these binding sites with similar affinities, which is consistent with the micromolar concn. of Hsts required for candidacidal activity. Specific 125I-Hst 5 binding was not detected to C. albicans spheroplasts, which were 14-fold less susceptible to Hst 5 killing, compared with intact cells in candidacidal assays. In overlay expts., 125I-Hst 5 bound to a 67-kDa protein detected in C. albicans whole cell lysates and crude membrane fractions, but not in the yeast cell wall fraction. Consistent with the overlay data, crosslinking of 125I-Hst 5 to C. albicans resulted in the appearance of a specific 73-kDa 125I-Hst 5-contg. complex that was not detected in the cell wall. 125I-Hst 5-binding protein of similar size was also obsd. in susceptible S. cerevisiae strain TI#20. This is the first description of Hst 5 binding sites on C. albicans which mediate cell killing and identification of a 67-kDa yeast Hst 5-binding protein. The binding characteristics of Hst 5 are in agreement with the obsd. potency of its biol. effect and provide crucial information to the use of Hst 5 as a therapeutic agent. The presence of a specific C. albicans Hst 5-binding protein provides further insight into the potential mechanism of yeast killing and suggests a basis for differential activity between yeast killing and the nontoxic nature of Hsts to humans.
RE.CNT 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 90 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:527193 CAPLUS
DN 129:166193
TI Therapeutic treatment and prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix
IN Setterstrom, Jean A.; Van Hamont, John E.; Reid, Robert H.; Jacob, Elliot; Jeyanthi, Ramasubbu; Boedeker, Edgar C.; McQueen, Charles E.; Tice, Thomas R.; Roberts, F. Donald; Friden, Phil
PA United States Dept. of the Army, USA; Van Hamont, John E.; et al.
SO PCT Int. Appl., 363 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 15 PATENT NO. KIND DATE APPLICATION NO. DATE ---
---------- ---- -------- ---------- --------
PI WO 9832427 A1 19980730 WO 1998-US1556 19980127 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG US 6309669 B1 20011030 US 1997-789734 19970127 AU 9863175 A1 19980818 AU 1998-63175 19980127
PRAI US 1997-789734 A 19970127 US 1984-590308 B1 19840316 US 1992-867301 A2 19920410 US 1995-446148 A2 19950522 US 1995-446149 B2 19950522 US 1996-590973 B2 19960124 WO 1998-US1556 W 19980127
AB Novel burst-free, sustained release biocompatible and biodegradable microcapsules are disclosed which can be programmed to release their active core for variable durations ranging from 1-100 days in an aq. physiol. environment. The microcapsules are comprised of a core of polypeptide or other biol. active agent encapsulated in a matrix of poly(lactide/glycolide) copolymer, which may contain a pharmaceutically acceptable adjuvant, as a blend of upcapped free carboxyl end group and end-capped forms ranging in ratios from 100/0 to 1/99.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 91 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:481400 CAPLUS
DN 129:199532
TI Structural features of the human salivary mucin, MUC7
AU Gururaja, Tarikere L.; Ramasubbu, Narayanan; Venugopalan, Paloth; Reddy, Molakala S.; Ramalingam, Kalaiyarasi; Levine, Michael J.
CS Department of Oral Biology and Research Center in Oral Biology, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Glycoconjugate Journal (1998), 15(5), 457-467 CODEN: GLJOEW; ISSN: 0282-0080
PB Chapman & Hall
DT Journal
LA English
AB Human salivary mucin (MUC7) is characterized by a single polypeptide chain of 357 aa. Detailed anal. of the derived MUC7 peptide sequence reveals five distinct regions or domains: (1) an N-terminal basic, ***histatin*** -like domain which has a leucine-zipper segment, (2) a moderately glycosylated domain, (3) six heavily glycosylated tandem repeats each consisting of 23 aa, (4) another heavily glycosylated MUC1- and MUC2-like domain, and (5) a C-terminal leucine-zipper segment. Chem. anal. and semi-empirical prediction algorithms for O-glycosylation suggested that 86/105 (83%) Ser/Thr residues were O-glycosylated with the majority located in the tandem repeats. The high (.apprx. 25%) proline content of MUC7 including 19 diproline segments suggested the presence of polyproline type structures. CD studies of natural and synthetic diproline-rich peptides and glycopeptides indicated that polyproline type structures do play a significant role in the conformational dynamics of MUC7. In addn., crystal structure anal. of a synthetic diproline segment (Boc-Ala-Pro-Pro-OBzl) revealed a polyproline type II extended structure. Collectively, the data indicate that the polyproline type II structure, dispersed throughout the tandem repeats, may impart a stiffening of the backbone and could act in consort with the glycosylated segments to keep MUC7 in a semi-rigid, rod shaped conformation resembling a "bottle-brush" model.
RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 92 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:412165 CAPLUS
DN 129:187154
TI The relationship between salivary ***histatin*** levels and oral yeast carriage
AU Jainkittivong, A.; Johnson, D. A.; Yeh, C. -K.
CS Department of Dental Diagnostic Science, University of Texas Health Science Center at San Antonio, San Antonio, USA
SO Oral Microbiology and Immunology (1998), 13(3), 181-187 CODEN: OMIMEE; ISSN: 0902-0055
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB Candida species are common commensal inhabitants of the oral cavity. Human saliva contains antifungal proteins called ***histatins*** . We tested the hypothesis that oral yeast status is related to salivary ***histatin*** levels. Thirty subjects were divided into two groups based on the presence (n=15) or absence (n=15) of yeast on oral mucosa surfaces. Unstimulated

and stimulated submandibular and sublingual and parotid saliva was collected from each subject. Salivary flow rates were measured and ***histatin*** concns. were detd. in the stimulated saliva samples. The yeast colony pos. group showed lower median unstimulated parotid saliva flow rates as well as lower median concns. of total ***histatins*** in submandibular and sublingual saliva. There was a neg. correlation between yeast colony-forming units and unstimulated parotid saliva flow rates and between yeast colony-forming units and submandibular and sublingual saliva ***histatin*** concn. and secretion. The results suggest that oral yeast status may be influenced by unstimulated parotid saliva flow rates and by submandibular and sublingual ***histatin*** concn. and secretion.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 93 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:274857 CAPLUS
DN 129:23433
TI ***Histatins*** for treatment of endotoxin-induced disorders
IN Kubogi, Yoshinori; Wang, Ho Rei
PA Japan Energy K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI JP 10114675 A2 19980506 JP 1996-270247 19961011
PRAI JP 1996-270247 19961011
AB Drugs for treatment of endotoxin-induced disorders, e.g. sepsis, contain ***histatins*** from human saliva proteins as active ingredients. Administration of ***histatin*** 5-contg. human saliva at 100 .mu.g/body reduced symptoms of endotoxin shock in mouse models in which activated macrophages were induced.

L3 ANSWER 94 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:222899 CAPLUS
DN 128:319630
TI Salivary proteins: a history and review
AU Khoo, Ks; Rahim, Zha
CS Department of Oral Biology, Faculty of Dentistry, University of Malaya, Kuala Lumpur, 50603, Malay.
SO Malaysian Journal of Biochemistry and Molecular Biology (1997), 1, 1-6 CODEN: MJBBF6
PB Malaysian Society for Biochemistry and Molecular Biology
DT Journal; General Review
LA English
AB A review with 53 refs. Salivary components perform many crucial roles in the oral cavity, including buffering, protection of the oral mucosa, digestion, pellicle formation, adhesion to bacteria, clearance of bacteria, bacteriostasis, bacteriolysis, lubrication and tannin-binding. With the exception of buffering which is principally due to inorg. ions, the other functions are facilitated by the presence of specific proteins in saliva. While a few salivary proteins, such as albumin and IgG, are passively transudated from the serum, most of them are saliva specific, being synthesized and secreted by the salivary glands. Some of the most abundant proteins in saliva are: the proline-rich proteins, which are involved in tannin-binding and pellicle formation; .alpha.-amylase, which besides being a pellicular constituent also causes bacterial clearance and the adhesion of streptococcal bacteria to the pellicle; mucoproteins which provides lubrication and secretory IgA which plays a role in immunol. protection. The proline-rich proteins which are the most significant, and perhaps the most intriguing group of proteins in saliva, are characterized by their high content of proline, glutamine and glycine, and a random coil conformation. Besides tannin-binding, they are also involved in the maintenance of calcium concn. in saliva. Much remains to be investigated regarding their effect on oral microflora and their possible role as mediators of taste. Other well-characterized salivary proteins include lysozyme, lactoferrin, statherin, ***histatins*** and cystatins. Lysozyme, lactoferrin and ***histatins*** have either bactericidal or bacteriostatic properties; while statherin is involved in maintaining supersatn. concns. of calcium in saliva, lastly cystatin is a protease inhibitor. Considering the richness of saliva as a source of biomols., the uniqueness of a no. of salivary proteins and the fact that more than a few of these are multifunctional, further studies may ascribe new roles and functions to these mols.
RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 95 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:103737 CAPLUS
TI Structure-function relationships in an antimicrobial salivary peptide: ***histatin*** -5
AU Melino, S.; Rufini, S.; Paci, M.; Petruzzelli, R.
CS Dip. Biol., Univ. "Tor Vergata", Rome, Italy
SO Italian Journal of Biochemistry (1997), 46(3), 158-159 CODEN: IJBIAC; ISSN: 0021-2938
PB Biomedia
DT Journal
LA English
AB Unavailable

L3 ANSWER 96 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:20346 CAPLUS
DN 128:189600
TI Structure of human salivary ***histatin*** 5 in aqueous and nonaqueous solutions
AU Raj, Periathamby Antony; Marcus, Emil; Sukumaran, Dinesh K.
CS Department of Oral Biology and Periodontal Disease Research Center, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Biopolymers (1998), 45(1), 51-67 CODEN: BIPMAA; ISSN: 0006-3525
PB John Wiley & Sons, Inc.
DT Journal
LA English
AB The soln. structure of human salivary ***histatin*** 5 was examd. in water (pH 3.8) and DMSO solns. using 500 MHz homo- and heteronuclear 2-dimensional (2D) NMR. The resonance assignment of peptide backbone and side-chain protons was accomplished by 2D total correlated spectroscopy and NOE spectroscopy. The high JNH-C.alpha.H values (.gtoreq.7.4 Hz), absence of any characteristic NH-NH(i, i + 1) or C.alpha.H-C.beta.H(i, i + 3) NOE connectivities, high d/dT values (.gtoreq.0.004 ppm K-1), and the fast 1H/2H amide exchange suggested that ***histatin*** 5 mols. remained unstructured in aq. soln. at pH 3.8. In contrast, ***histatin*** 5 preferred largely an .alpha.-helical conformation in DMSO soln. as evident from the JNH-C.alpha.H values (.ltoreq.6.4 Hz), slow 1H/2H exchange, low d/dT values (.ltoreq.0.003 ppm K-1) obsd. for amide resonances of residues 6-24, and the characteristic NH-NH(i, i + 1) and C.alpha.H-C.beta.H(i, i + 3) NOE connectivities. All backbone amide 15N-1H connectivities fell within 6 ppm on the 15N scale in the 2D heteronuclear single quantum correlated spectrum, and the restrained structure calcns. using DIANA suggested the prevalence of .alpha.-helical conformations stabilized by 19 (5 .fwdarw. 1) intramol. backbone amide H-bonds in polar aprotic medium such as DMSO. The interside-

chain H-bonding and salt-bridge type interactions that normally stabilize the helical structure of linear peptides in aq. solns. were not obsd. ***Histatin*** 5, unlike other naturally occurring antimicrobial polypeptides such as magainins, defensins, and tachyplesins, did not adopt amphiphilic structure, precluding its insertion into microbial membranes and formation of ion channels across membranes. Electrostatic (ionic type) and H-bonding interactions of the pos. charged and polar residues with the head groups of microbial membranes or with a membrane-bound receptor could be the initial step involved in the mechanism of antimicrobial activity of ***histatins*** .
RE.CNT 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 97 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:710861 CAPLUS
DN 127:356433
TI Characterization of human sublingual-gland protein kinase by phosphorylation of a peptide related to secreted proteins
AU Nam, Yesi; Madapallimattam, George; Drzymala, L.; Bennick, Anders
CS Department of Biochemistry, University of Toronto, Toronto, M5S 1A8, Can.
SO Archives of Oral Biology (1997), 42(8), 527-537 CODEN: AOBIAR; ISSN: 0003-9969
PB Elsevier
DT Journal
LA English
AB Phosphoproteins in human saliva include proline-rich proteins, statherins, ***histatin*** 1 and cystatin SA-III. The presence of phosphate in these proteins is necessary for various functions in the mouth including calcium binding, inhibition of pptn. of calcium phosphate, inhibition of growth of hydroxyapatite crystals and adherence to hydroxyapatite. To elucidate the process of phosphorylation of these proteins, the phosphorylation of a peptide (APR8) with an amino acid sequence identical to one of the phosphorylated sites in acidic proline-rich proteins by a kinase from the human sublingual gland was investigated. The kinase, which was highly labile, was purified 58-fold by fractionation of sublingual gland homogenate and gel filtration, but the enzyme was inactivated when further purifn. by chromatog. techniques commonly used for protein kinases was attempted. To compare the enzyme with other kinases, and to obtain information that could be used in its further purifn., a characterization was undertaken. The enzyme required 10 mM Mg2+ for optimum activity, it had a KM of 0.09 mM for ATP and the KM for the peptide substrate APRP8 was 0.42 mM. It was not activated by cAMP or calmodulin, characteristics that are shared with casein kinases and mammary gland kinase. The sublingual kinase as well as casein kinase 2 were inhibited by heparin, but in other respects the two kinases had different properties. While casein kinase 2 is activated by polylysine and has optimal activity in 150 mM KCl, sublingual kinase was inhibited by polylysine and the addn. of KCl. Moreover, casein kinase 2 can utilize both ATP and GTP as phosphoryl donors, but GTP was not a substrate for sublingual kinase. The sublingual kinase shared a substrate recognition sequence with mammary gland kinase, but, unlike that kinase, it could not utilize Ca2+ instead of Mg2+. While the sublingual kinase thus shared some properties with both casein kinase 2 and mammary gland kinase, distinct differences were also seen and the relationship to these enzymes remains to be detd. The characterization of the sublingual kinase will be useful in its further purifn.

L3 ANSWER 98 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:660417 CAPLUS
DN 127:356902
TI Studies of the mechanism of human salivary ***histatin*** -5 candidacidal activity with ***histatin*** -5 variants and azole-sensitive and -resistant Candida species
AU Tsai, Hsiaoyun; Bobek, Libuse A.
CS Department of Oral Biology, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Antimicrobial Agents and Chemotherapy (1997), 41(10), 2224-2228 CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB ***Histatins*** are a group of small, cationic, antifungal peptides present in human saliva. A previous mol. modeling anal. suggested structural similarity between the Phe14-His15 and His18-His19 dipeptide sequences in ***histatin*** -5 (Hsn-5; a 24-amino-acid polypeptide) and the sequence of miconazole (one of the azole-based antifungal therapeutic agents), implying that the mechanisms of killing of Candida albicans by these two mols. may be similar. To further elaborate on this observation, we have produced two variants of Hsn-5 in which Phe14-His15 or His18-His19 dipeptide sequences were replaced by Ala-Ala (F14A/H15A and H18A/H19A) to eliminate the Ph and imidazole rings of the side chains and assessed their candidacidal activities against C. albicans. In addn., we tested azole-resistant C. albicans and Candida glabrata strains for their susceptibilities to Hsn-5. Anal. of the purified recombinant proteins for their candidacidal activities indicated that both variants were significantly less effective (the molar concns. required to kill half of the max. no. of cells [ED50s], .apprx.67 and .apprx.149 .mu.M for F14A/H15A and H18A/H19A, resp.) than the unaltered Hsn-5 (ED50, .apprx.8 .mu.M) at killing C. albicans, suggesting that the two dipeptide sequences are important for the candidacidal activity of Hsn-5. Assessment of the candidacidal activity of Hsn-5 with the well-characterized azole-resistant strains of C. albicans and C. glabrata, however, suggested that the mode of action of ***histatins*** against Candida is distinct from that of azole-based antifungal agents because Hsn-5 kills both azole-sensitive and azole-resistant strains equally well.

L3 ANSWER 99 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:616253 CAPLUS
DN 127:306556
TI Human salivary ***histatin*** -5 exerts potent fungicidal activity against Cryptococcus neoformans
AU Tsai, Hsiaoyun; Bobek, Libuse A.
CS Department of Oral Biology, School of Dental Medicine, State University of New York at Buffalo, 202 Foster Hall, Buffalo, NY, 14214, USA
SO Biochimica et Biophysica Acta (1997), 1336(3), 367-369 CODEN: BBACAQ; ISSN: 0006-3002
PB Elsevier
DT Journal
LA English
AB Human salivary ***histatins*** (Hsns) have been known to be potent antifungal agents against Candida albicans for more than a decade. Here, the authors report that Hsns are also effective in killing another medically important opportunistic fungal pathogen, Cryptococcus neoformans, which has become a new threat among the immunocompromised patients, esp. AIDS patients. In fact, the cidal activity of Hsn-5 against C. neoformans is as high as that against C. albicans.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 100 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:594224 CAPLUS
DN 127:275206

TI Synthetic ***histatin*** analogs with broad-spectrum antimicrobial activity
AU Helmerhorst, Eva J.; Van 't Hof, Wim; Veerman, Enno C. I.; Simoons-Smit, Ina; Nieuw Amerongen, Arie V.
CS Department of Oral Biochemistry, Vrije Universiteit, ACTA, Amsterdam, 1081 BT, Neth.
SO Biochemical Journal (1997), 326(1), 39-45 CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press
DT Journal
LA English
AB ***Histatins*** are salivary histidine-rich cationic peptides, ranging from 7 to 38 amino acid residues in length, that exert a potent killing effect in vitro on Candida albicans. Starting from the C-terminal fungicidal domain of ***histatin*** 5 (residues 11-24, called dh-5) a no. of substitution analogs were chem. synthesized to study the effect of amphipathicity of the peptide in helix conformation on candidacidal activity. Single substitutions in dh-5 at several positions did not have any effect on fungicidal activity. However, multi-site substituted analogs (dhvar1 and dhvar2) exhibited a 6-fold increased activity over dh-5. In addn., dhvar1 and dhvar2 inhibited the growth of the second most common yeast found in clin. isolates, Torulopsis glabrata, of oral- and non-oral pathogens such as Prevotella intermedia and Streptococcus mutans, and of a methicillin-resistant Staphylococcus aureus. In their broad-spectrum activity, dhvar1 and dhvar2 were comparable to magainins (PGLa and magainin 2), antimicrobial peptides of amphibian origin. Both the fungicidal and the hemolytic activities of dhvar1, dhvar2 and magainins increased at decreasing ionic strength.

L3 ANSWER 101 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:533928 CAPLUS
DN 127:159387
TI Applied biotechnology for dentistry. Application of biotechnology to the research and clinical trial on salivary function
AU Minaguchi, Kiyoshi
CS Dep. Forensic Odontol., Tokyo Dent. Coll., Chiba, 261, Japan
SO Shika Gakuho (1997), 97(6), 589-596 CODEN: SHGKA3; ISSN: 0037-3710
PB Tokyo Shika Daigaku Gakkai
DT Journal; General Review
LA Japanese
AB A review with 24 refs. Introduction of aquaporin 1 gene to salivary gland of rat increases secretion of saliva as model of Sjogren syndrome. ***Histatin*** secretion to saliva is elevated by introduction of human ***histatin*** 3 gene to rat salivary gland, which is a model therapy of Candida albicans infection frequently obsd. in Sjogren syndrome using binding activity of ***histatin*** to C. albicans. Development of biotechnol. have elucidated genes of salivary proteins. Biotechnol. enables us to elucidate functional difference of products with gene polymorphism, gene expression regulation and artificial control of gene expression.

L3 ANSWER 102 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:513551 CAPLUS
DN 127:181162
TI Novel burst-free sustained release poly(lactide/glycolide) microspheres
IN Jeyanthi, Ramasubbu; Van Hamont John F.; Friden, Phil; Reid, Robert H.; Roberts, F. Donald; McQueen, Charles E.; Setterstrom, Jean A.
PA United States Dept. of the Army, USA; Jeyanthi, Ramasubbu; Van Hamont, John F.; Friden, Phil; Reid, Robert H.; Roberts, F. Donald; McQueen, Charles E.; Setterstrom, Jean A.
SO PCT Int. Appl., 51 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 15 PATENT NO. KIND DATE APPLICATION NO. DATE ---
PI WO 9726869 A1 19970731 WO 1996-US19440 19961118 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG CA 2216371 AA 19970731 CA 1996-2216371 19961118 AU 9714104 A1 19970820 AU 1997-14104 19961118 AU 722884 B2 20000810 EP 817619 A1 19980114 EP 1996-944247 19961118 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI CN 1188408 A 19980722 CN 1996-194768 19961118 JP 11509862 T2 19990831 JP 1996-526833 19961118 BR 9607752 A 19991130 BR 1996-7752 19961118 NZ 335409 A 20001222 NZ 1996-335409 19961118
PRAI US 1996-590973 A 19960124 NZ 1996-325561 A1 19961118 WO 1996-US19440 W 19961118
AB Novel burst-free, sustained release biocompatible and biodegradable microcapsules which can be programmed to release their active core for variable durations ranging from 1-100 days in an aq. physiol. environment. The microcapsules are comprised of a core of polypeptide or other biol. active agent encapsulated in a matrix of poly(lactide/glycolide) copolymer as a blend of uncapped (free carboxyl end group) and end-capped forms ranging in ratios from 100/0 to 1/99.

L3 ANSWER 103 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:504558 CAPLUS
DN 127:216879
TI Histidine-rich human salivary peptides are inhibitors of proprotein convertases furin and PC7 but act as substrates for PC1
AU Basak, Ajoy; Ernst, Blair; Brewer, Dyanne; Seidah, Nabil G.; Munzer, Jon S.; Lazure, Claude; Lajoie, Gilles A.
CS Laboratories of Structure and Metabolism of Neuropeptides, Clinical Research Institute of Montreal, Montreal, QC, Can.
SO Journal of Peptide Research (1997), 49(6), 596-603 CODEN: JPERFA; ISSN: 1397-002X
PB Munksgaard
DT Journal
LA English
AB A 32 amino acid peptide called ***histatin*** -3 (H3; 22% His) and its N-terminal 24 amino acid fragment ***histatin*** -5 (H5, 33% His), are found in human saliva and possess powerful antimicrobial properties. These His-rich peptides have been synthesized by Fmoc-based solid-phase chem. Their sequences are: DSHAKRHHGYKRKFHEKHHSHRGYRSNYLYDN (H3) and DSHAKRHHGYKRKFHEKHHSHRGY (H5). In addn., we also prepd. two H5 and one H3 mutants. The H5 mutants were: DH5 (all amino acids in D configuration) and H5F (where all His are replaced by Phe at positions 3, 7, 8, 15, 18, 19, 21). The 9-24 segment of H3 with all the His at positions 15, 18, 19, 21 replaced by Tyr was also prepd. (.DELTA.1-8H3Y). The behavior of these five peptides was examd. with three proprotein convertases (PC's) which possess cleavage specificity directed towards single and pairs of basic residues. These were: human (h)PC1, an endocrine and neural convertase, hfurin and rat (r)PC7, two widely expressed enzymes. All are serine endoproteases belonging to the kexin/subtilisin family. Our in vitro study revealed that H3 behaves as a substrate for PC1, being cleaved by this endoprotease primarily at a site carboxy

terminal to the single Arg25 residue (HRGYRSN). On prolonged incubation some minor cleavage was also obsd. C-terminal to the first LysArg6 pairs of basic amino acids namely at: HAKRHH, which contains a P4 as well as P'1 and P'2 His residues. The second potential site YKRK12-FH which does not have a P4 basic residues is not cleaved, even upon incubation with excess protease. PC1 only poorly cleaves H5 at the same site mentioned above for H3, i.e., at HAKRHH. As expected, neither the D-amino acid analog (DH5), nor the Phe and Tyr mutant analogs of the long and short ***histatins*** , resp., are cleaved at all. In contrast to the above findings for hPC1, the convertase hfurin did not cleave any of the five synthetic peptides. Instead, H3 and H5 were found to be moderately potent inhibitors of the furin-mediated cleavage of the pentapeptide pGlu-Arg-Thr-Lys-Arg-MCA fluorogenic substrate. This inhibition was reversible and competitive, with an estd. inhibition const. Ki of 1.98 .mu.M for H3 and 2.98 .mu.M for H5. The other analogs exhibited only a moderate to weak inhibition of furin, suggesting that substitution of all His by arom. residues (Phe or Tyr) drastically reduces their inhibitory potency. When tested against rPC7, H3 exhibited almost identical inhibition profile with a measured Ki of 2.4 .mu.M. The partial sequence identity of H3 to the inhibitory pro-peptide of furin and PC7 provides a rationale for our observation.

L3 ANSWER 104 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:492789 CAPLUS
DN 127:130985
TI D-amino acid ***histatin*** -based peptides as antifungal and antibacterial agents
IN Oppenheim, Frank G.; Xu, Tao; Spacciapoli, Peter
PA Periodontix, Inc., USA; Trustees of Boston University
SO U.S., 23 pp., Cont.-in-part of U.S. 5,486,503. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI US 5646119 A 19970708 US 1995-485273 19950607 US 5486503 A 19960123 US 1994-287717 19940809 CA 2221780 AA 19961219 CA 1996-2221780 19960607 WO 9640770 A2 19961219 WO 1996-US9962 19960607 WO 9640770 A3 19970206 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA AU 9661696 A1 19961230 AU 1996-61696 19960607 AU 711526 B2 19991014 EP 832120 A2 19980401 EP 1996-919334 19960607 EP 832120 B1 20020220 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 11507376 T2 19990629 JP 1996-502116 19960607 AT 213500 E 20020315 AT 1996-919334 19960607 ES 2170239 T3 20020801 ES 1996-919334 19960607 US 5885965 A 19990323 US 1998-973563 19980312
PRAI US 1991-786571 B1 19911101 US 1993-145030 B1 19931028 US 1994-287717 A2 19940809 US 1995-485273 A 19950607 WO 1996-US9962 W 19960607
AB D-amino acid ***histatins*** and ***histatin*** -based peptides, ***histatins*** , and methods for treatment of fungal or bacterial infection are described. These D-amino acid ***histatins*** and ***histatin*** -based peptides are longer-acting anti-fungal or anti-bacterial agents than their L-enantiomeric analogs.

L3 ANSWER 105 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:474522 CAPLUS
DN 127:145830
TI An expanded ***histatin*** gene polymorphism and test of a possible disease resistant phenotype
AU Araki, Motohide; Anstey, Nicholas M.; Mwaikambo, Esther D.; Dua, Arnavaz; Amberger, Ed; Azen, Edwin A.
CS Department of Orthodontics, ASAHI University School of Dentistry, Motosu-G, 501-02, Japan
SO Human Mutation (1997), 10(1), 58-64 CODEN: HUMUE3; ISSN: 1059-7794
PB Wiley-Liss
DT Journal
LA English
AB ***Histatins*** are small mol. wt. salivary proteins that are important in the non-immune host defense system. Two frequent cis-linked coding-change mutations were previously described in exon 5 of the HIS2 gene of blacks. The polymorphic mutant allele was termed HIS22 and the wild-type allele HIS21. We here describe two new non-coding change polymorphisms of the HIS2 gene: a deletion in intron 5 (7183-7198 del) and a C.fwdarw.T mutation in exon 5 [C.fwdarw.T (7104)] that characterize two new HIS2 alleles, HIS23 and HIS24 resp. Both mutations occur on a HIS21 background. The HIS23 allele occurred only in Afro-Americans, but not in 67 Japanese, 51 Chinese and 50 Whites. Among 66 random DNA samples from Afro-Americans, frequencies of HIS21, HIS22, HIS23 and HIS24 were 0.67, 0.22, 0.05 and 0.07 resp., with a heterozygosity of 0.45. The frequencies of the HIS24 allele in 50 Whites and 50 Chinese were 0.06, and 0.1 resp. In a comparison of 60 matched saliva and DNA samples from the Afro-American population, the DNA-based mutation anal. reliably identified salivary ***histatin*** phenotypes. The salivary ***histatin*** polymorphism (inferred from PCR anal.) was used to test a biol. plausible hypothesis, that the mutant ***histatin*** phenotype (coded by the HIS22 allele) confers relative resistance to severe and fatal malaria. In a study of 185 Black Tanzanian subjects, there were no significant differences in HIS22 allelic frequencies between the various test groups: for 86 cerebral malaria subjects, 54 uncomplicated malaria subjects, and 45 combined asymptomatic parasitemia and health controls, HIS22 frequencies were 0.16, 0.17 and 0.17 resp. Thus, there was no support for the hypothesis in this population.

L3 ANSWER 106 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:463886 CAPLUS
DN 127:126494
TI One-month controlled release of an antimicrobial peptide from biodegradable poly(lactide/glycolide) microspheres for the treatment of periodontitis
AU Jeyanthi, R.; Akiyama, A.; Roberts, F.D.; Van Hamont, J.; Friden, P.
CS Periodontix Inc., Watertown, MA, 02172, USA
SO Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1997), 24th, 883-884 CODEN: PCRMEY; ISSN: 1022-0178
PB Controlled Release Society, Inc.
DT Journal
LA English
AB A 1-mo controlled-release formulation using a low mol.-wt. uncapped glycolide-lactide copolymer was developed for the antimicrobial peptide, ***histatin*** P-113 for the treatment of periodontitis. The peptide released from the microspheres prepd. without additives was not bioactive. The bioactivity was maintained at 100% by the addn. of a nonionic surfactant Poloxamer 407.

L3 ANSWER 107 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:455438 CAPLUS
DN 127:78992

TI ***Histatins*** : structure, function, and genetics: current understanding and future perspectives
AU Driscoll, James; Xu, Tao; Oppenheim, Frank G.
CS Department of Periodontology and Oral Biology, Goldman School of Graduate Dentistry, Boston University Medical Center, Boston, MA, 02118, USA
SO Studies in Stomatology and Craniofacial Biology (1997), 445-460. Editor(s): Cohen, M. Michael, Jr.; Baum, Bruce J. Publisher: IOS Press, Amsterdam, Neth. CODEN: 64SKAK
DT Conference; General Review
LA English
AB A review and discussion with many refs. on the biochem. isolation and functional characterization, primary structure, anticandidal activity, evolutionary relationship of salivary ***histatins*** in anthropoid primates, mol. genetics of the ***histatins*** , genetic regulations and gene therapy were discussed.

L3 ANSWER 108 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:418509 CAPLUS
DN 127:60197
TI Structure-function studies of human salivary ***histatins*** with respect to their candidacidal activity
AU Tsai, Hsiaoyun
CS State Univ. of New York, Buffalo, NY, USA
SO (1997) 135 pp. Avail.: UMI, Order No. DA9719183 From: Diss. Abstr. Int., B 1997, 58(1), 151
DT Dissertation
LA English
AB Unavailable

L3 ANSWER 109 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:406056 CAPLUS
DN 127:16799
TI Enzymic fungicides for foods and cosmetics
IN Brul, Stanley; Coote, Peter; Dielbanhoesing, Shanti; Oomes, Suzanna; Stam, Wilma M.; Naaktgeboren-stoffels, Geke; Stratford, Malcolm
PA Unilever N.V., Neth.; Unilever Plc
SO PCT Int. Appl., 24 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9716973 A2 19970515 WO 1996-EP4727 19961030 WO 9716973 A3 19970731 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG CA 2236223 AA 19970515 CA 1996-2236223 19961030 CA 2236223 C 20020806 AU 9674961 A1 19970529 AU 1996-74961 19961030 AU 728379 B2 20010111 EP 876102 A2 19981111 EP 1996-937303 19961030 EP 876102 B1 20010620 R: BE, DE, DK, FR, GB, NL, SE, IE, FI HU 219315 B 20010328 HU 1999-92 19961030 CZ 289415 B6 20020116 CZ 1998-1337 19961030 ZA 9609181 A 19980430 ZA 1996-9181 19961031 US 5888504 A 19990330 US 1996-742730 19961101 PRAI EP 1995-202977 A 19951103 EP 1995-202978 A 19951103 EP 1995-202979 A 19951103 WO 1996-EP4727 W 19961030
AB The title fungicides comprise fungal cell wall lytic enzymes (chitinase, .beta.-1,3-glucanase, .beta.-1,6-glucanase) and a natural microbial cell membrane affecting substance, such as nisin and an amphiphilic .alpha.-helix-forming peptides, or herbal substances.

L3 ANSWER 110 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:366667 CAPLUS
DN 127:44955
TI Antifungal and antibacterial ***histatin*** -based peptides
IN Oppenheim, Frank G.; Xu, Tao; Roberts, F. Donald
PA Periodontix, Inc., USA; Boston University
SO U.S., 21 pp., Cont.-in-part of U.S. 5,486,503. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI US 5631228 A 19970520 US 1995-481888 19950607 US 5486503 A 19960123 US 1994-287717 19940809 CA 2223505 AA 19961219 CA 1996-2223505 19960607 WO 9640768 A2 19961219 WO 1996-US9374 19960607 WO 9640768 A3 19970306 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA AU 9661585 A1 19961230 AU 1996-61585 19960607 AU 709204 B2 19990826 EP 832119 A2 19980401 EP 1996-919182 19960607 EP 832119 B1 20000920 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 11508238 T2 19990721 JP 1996-501707 19960607 AT 196475 E 20001015 AT 1996-919182 19960607 ES 2151172 T3 20001216 ES 1996-919182 19960607 US 5912230 A 19990615 US 1998-973559 19980311
PRAI US 1991-786571 B1 19911101 US 1993-145030 B1 19931028 US 1994-287717 A2 19940809 US 1995-481888 A 19950607 WO 1996-US9374 W 19960607
AB ***Histatin*** -based peptides representing defined portions of the amino acid sequences of naturally occurring human ***histatins*** and methods for treatment of fungal or bacterial infection are described. These ***histatin*** -based peptides represent the active anti-fungal and anti-bacterial region of naturally occurring human ***histatins*** .

L3 ANSWER 111 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:302099 CAPLUS
DN 127:28650
TI Inhibition of experimental gingivitis in beagle dogs with topical salivary ***histatins***
AU Paquette, D. W.; Waters, G. S.; Stefanidou, V. L.; Lawrence, H. P.; Friden, P. M.; O'connor, S. M.; Sperati, J. D.; Oppenheim, F. G.; Hutchens, L. H.; Williams, R. C.
CS Departments of Periodontics, University of North Carolina School of Dentistry, Chapel Hill, NC, USA
SO Journal of Clinical Periodontology (1997), 24(4), 216-222 CODEN: JCPEDZ; ISSN: 0303-6979
PB Munksgaard
DT Journal
LA English
AB ***Histatins*** , histidine-rich proteins found within parotid and submandibular secretions, are a novel class of endogenous peptides with antimicrobial properties. This masked, randomized, placebo-controlled preclin. investigation examd. the effect of 3 topical ***histatins*** on the development of plaque and gingivitis in beagle dogs. 16, Female, 1-yr-old beagles were brought to optimal gingival health by mech. scaling and polishing followed by rigorous daily tooth brushing. At the conclusion of this pretreatment period, dogs were randomly divided into 4 groups for the application of test formulations, and were placed on a plaque-promoting diet. Test agents included 3 synthetic salivary ***histatins*** (***histatin*** 5, P-113 and P-113D)

which were incorporated in hydroxypropyl Me cellulose gel at a concn. of 0.125%, and a placebo, or neg. control, which was the gel vehicle alone. Throughout the 10-wk treatment period, test formulations (2.0 mL) were applied 2.times.daily to all premolar teeth using a Monojet syringe. Plaque formation and gingival inflammation were assessed using the plaque (PI) and gingival (GI) indexes on days 0, 7, 14, 21, 28, 42, 56 and 70. Furthermore, bleeding to probing was recorded as a percent of sites (%BOP) and according to the modified sulcus bleeding index (mSBI). Comparisons among groups and between group pairs (active vs. placebo) were made with Kruskal-Wallis tests with the av. of data over the interval, days 14-42, being the primary focus of the anal. From baseline to day 7, all groups expressed similar indexes. Thereafter, overall significant differences among the groups were noted at day 42 for PI, at days 21, 28, 42 and 70 for GI, and at days 14 and 28 for %BOP. In particular, beagles treated with P-113 demonstrated significantly lower PI scores at day 42, significantly lower GI scores from days 21 through 42, and significantly lower %BOP scores at days 14 and 28 compared to beagles treated with placebo. Beagles treated with P-113D exhibited significantly lower GI at day 42 compared to the placebo. For the primary anal. conducted over the midtreatment interval (days 14-42), significant differences were detected for all parameters except mSBI. Accordingly, significantly lower PI scores were found for P-113, lower GI scores for P-113 and P-113D, and lower %BOP for P-113 and P-113D compared to placebo. These data indicate that in the beagle model, salivary ***histatins*** , P-113 and P-113D, topically applied, can significantly reduce clin. signs of plaque formation and gingival inflammation.

L3 ANSWER 112 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:287089 CAPLUS
DN 126:340694
TI Human salivary mucin MG1 selectivity forms heterotypic complexes with amylase, proline-rich proteins, statherin, and ***histatins***
AU Iontcheva, I.; Oppenheim, F. g.; Troxler, R. F.
CS Dep. Periodontol. Oral Biol., Sch. Dental Med., Boston Univ. Sch. Med., Boston Univ. Med. Cent., Boston, MA, 02118, USA
SO Journal of Dental Research (1997), 76(3), 734-743 CODEN: JDREAF; ISSN: 0022-0345
PB International Association for Dental Research
DT Journal
LA English
AB Heterotypic complexes between the high-mol.-wt. mucin MG1 and other salivary proteins in human submandibular/sublingual secretion (HSMSL) could have a significant impact on the biol. properties of these proteins in oral fluids in both health and disease. We describe a mild procedure for isolation and purifn. of native MG1 by gel filtration chromatog. on Sepharose CL-2B which does not involve dialysis, lyophilization, use of denaturing agents, or covalent modification. Western blots of native MG1 probed with antibodies against 8 different salivary proteins showed that complexing occurs between MG1 and salivary amylase, proline-rich proteins (PRPs) statherins, and ***histatins*** but not MG1, sIgA, secretory component, or crystatins. When native MG1 was placed in 4 M guanidine hydrochloride and chromatographed on Sepharose CL-4B, ELISA measurement of column fractions showed that amylase, PRPs, statherins, and ***histatins*** were released. Interestingly, gel filtration resolved the material which eluted into 4 or 5 distinct peaks, suggesting that the released entities were heterotypic complexes. From these studied, the occurrence of at least three different types of complexes between MG1 and other salivary proteins has been identified. Type I complexes are dissocd. by SDS-PAGE and in 4 M guanidine hydrochloride. Type II complexes are not dissocd. under these conditions. Type III complexes are dissocd. during SDS-PAGE and by 4 M guanidine hydrochloride, but the released proteins appear to be complexes contg. amylase, PRPs, statherins, and ***histatins*** . The possible functional role of heterotypic complexes between MG1 and other salivary proteins as a physiol. delivery system, a mechanism for protection against proteolysis, a respiratory for precursors of the acquired enamel pellicle, and a vesicle for modulation of the viscoelastic and rheol. properties of saliva is discussed.

L3 ANSWER 113 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:125931 CAPLUS
DN 126:222738
TI Effect of acetylation and permethylation on the conformation and candidacidal activity of salivary ***histatin*** -5
AU Ramalingam, Kalaiyarasi; Ramasubbu, Narayanan; Levine, Michael J.
CS Department of Oral Biology, School of Dental Medicine, State University of New York at Buffalo, Buffalo, NY, 14214, USA
SO Letters in Peptide Science (1997), 3(6), 349-356 CODEN: LPSCEM; ISSN: 0929-5666
PB ESCOM
DT Journal
LA English
AB Salivary ***histatins*** provide a non-immune defense against oral pathogens such as Candida albicans. The structural requirements of ***histatin*** -5 for anticandida activity were examd. with respect to its ability to adopt helical structures, its electrostatic interactions and the hydrogen-bonding potency of its basic residues. For this purpose, the lysine and/or histidine residues of ***histatin*** -5 were chem. modified by acetylation and permethylation. Acetylated ***histatin*** -5 retained its ability to adopt helical structures in 2,2,2-trifluoroethanol, but completely lost its ability to kill yeast cells. In contrast, permethylated ***histatin*** -5 shows very little tendency to adopt a helical structure, but retained significant anticandida activity. The results suggest that the candidacidal activity can arise even when the ***histatin*** does not have the ability to adopt helical structures. The candidacidal activity of the derivs. is discussed in terms of electrostatic interactions and hydrogen-bonding potency.

L3 ANSWER 114 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:116549 CAPLUS
DN 126:113162
TI Anti-fungal and anti-bacterial ***histatin*** -based peptides
IN Oppenheim, Frank G.; Xu, Tao; Roberts, F. Donald; Spacciapoli, Peter; Friden, Phillip M.
PA Periodontix, Inc., USA; Trustees of Boston University; Oppenheim, Frank G.; Xu, Tao; Roberts, F. Donald; Spacciapoli, Peter; Friden, Phillip M.
SO PCT Int. Appl., 70 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9640768 A2 19961219 WO 1996-US9374 19960607 WO 9640768 A3 19970306 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA US 5631228 A 19970520 US 1995-481888 19950607 AU 9661585 A1 19961230 AU 1996-61585 19960607 AU 709204 B2 19990826 EP 832119 A2 19980401 EP 1996-919182 19960607 EP 832119 B1 20000920 R:

AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 11508238 T2 19990721 JP 1996-501707 19960607 AT 196475 E 20001015 AT 1996-919182 19960607 US 5912230 A 19990615 US 1998-973559 19980311
PRAI US 1995-481888 A 19950607 US 1991-786571 B1 19911101 US 1993-145030 B1 19931028 US 1994-287717 A2 19940809 WO 1996-US9374 W 19960607
OS MARPAT 126:113162
AB ***Histatin*** -based peptides representing defined portions of the amino acid sequences of naturally occurring human ***histatins*** and methods for treatment of fungal or bacterial infection are described. These ***histatin*** -based peptides represent the active anti-fungal and anti-bacterial region of naturally occurring human ***histatins*** .

L3 ANSWER 115 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:107449 CAPLUS
DN 126:113161
TI ***Histatin*** derivatives containing D-amino acids for use as antifungals and antibacterials
IN Oppenheim, Frank G.; Xu, Tao; Spacciapoli, Peter; Roberts, F. Donald; Friden, Phillip M.
PA Periodontix, Inc., USA; Trustees of Boston University; Oppenheim, Frank G.; Xu, Tao; Spacciapoli, Peter; Roberts, F. Donald; Friden, Phillip M.
SO PCT Int. Appl., 61 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 7 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9640770 A2 19961219 WO 1996-US9962 19960607 WO 9640770 A3 19970206 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA US 5646119 A 19970708 US 1995-485273 19950607 AU 9661696 A1 19961230 AU 1996-61696 19960607 AU 711526 B2 19991014 EP 832120 A2 19980401 EP 1996-919334 19960607 EP 832120 B1 20020220 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI JP 11507376 T2 19990629 JP 1996-502116 19960607 AT 213500 E 20020315 AT 1996-919334 19960607 US 5885965 A 19990323 US 1998-973563 19980312
PRAI US 1995-485273 A 19950607 US 1991-786571 B1 19911101 US 1993-145030 B1 19931028 US 1994-287717 A2 19940809 WO 1996-US9962 W 19960607
AB ***Histatin*** derivs. contg. D-amino acids and methods for treatment of fungal or bacterial infection are described. These D-amino acid ***histatins*** and ***histatin*** derivs. are longer-acting anti-fungal or anti-bacterial agents than their L-enantiomeric analogs.

L3 ANSWER 116 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:28569 CAPLUS
DN 126:69770
TI Transfer of a gene encoding the anticandidal protein ***histatin*** 3 to salivary glands
AU O'Connell, Brian C.; Xu, Tao; Walsh, Thomas J.; Sein, Tin; Mastrangeli, Andrea; Crystal, Ronald G.; Oppenheim, Frank G.; Baum, Bruce J.
CS Clinical Investigations and Patient Care Branch, National Institute of Dental Research, National Institutes of Health, Bethesda, MD, 20892, USA
SO Human Gene Therapy (1996), 7(18), 2255-2261 CODEN: HGTHE3; ISSN: 1043-0342
PB Liebert
DT Journal
LA English
AB Mucosal candidiasis, the most common opportunistic fungal infection in human immunodeficiency virus (HIV)-infected patients, is an early sign of clin. overt acquired immunodeficiency syndrome (AIDS) and an important cause of morbidity, particularly in HIV-infected children. The appearance of azole-resistant strains of Candida albicans had made clin. management of candidiasis increasingly difficult. We propose a novel approach to the management of candidal infections that involves the use of naturally occurring antifungal proteins, such as the ***histatins*** . ***Histatins*** are a family of small proteins that are secreted in human saliva. We have constructed recombinant adenovirus vectors that contain the ***histatin*** 3 cDNA. These vectors are capable of directing the expression of ***histatin*** 3 in the saliva of rats at up to 1,045 .mu.g/mL, well above the levels found in normal human saliva. The adenovirus-directed ***histatin*** demonstrated a 90% candidacidal effect in the timed-kill assay against both fluconazole-susceptible and fluconazole-resistant strains of C. albicans and inhibited germination by 45% in the same strains. These studies suggest that a gene transfer approach to over-express naturally occurring antifungal proteins may be useful in the management of mucosal candidiasis.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 117 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:718607 CAPLUS
DN 126:6402
TI Candidacidal activity of recombinant human salivary ***histatin*** -5 and variants
AU Tsai, Hsiaoyun; Raj, Periathamby Antony; Bobek, Libuse A.
CS Dep. Oral Biol., State Univ. New York, Buffalo, NY, 14214, USA
SO Infection and Immunity (1996), 64(12), 5000-5007 CODEN: INFIBR; ISSN: 0019-9567
PB American Society for Microbiology
DT Journal
LA English
AB Human salivary ***histatins*** possess fungicidal and bactericidal activities. The current investigation evaluates the structure-function relation of ***histatins*** with regard to their candidacidal activity by using recombinant ***histatin*** -5 and its variants produced in Escherichia coli. The purified recombinant ***histatins*** were examd. for their candidacidal activity and secondary structure. The m21 (with Lys-13 replaced by Thr [Lys-13.fwdarw.Thr]) and m71 (Lys-13.fwdarw.Glu) variants are less effective than recombinant ***histatin*** -5 in killing Candida albicans, suggesting that Lys-13 is crit. for candidacidal activity. The m68 (Lys-13.fwdarw.Glu and Arg-22.fwdarw.Gly) variant is less potent than the recombinant ***histatin*** -5 as well as m71, indicating that Arg-22 is crucial for the candidacidal activity. The candidacidal activities of m1 (Arg-12.fwdarw.Ile), m2 (Arg-12.fwdarw.Ile and Lys-17.fwdarw.Asp), m12 (Arg-12.fwdarw.Lys and His-21.fwdarw.Leu), and m70 (His-19.fwdarw.Pro and His-21.fwdarw.Arg) variants, however, are comparable to that of recombinant ***histatin*** -5, indicating that Arg-12, Lys-17, His-19, and His-21 are not functionally important. The conformational preferences of ***histatin*** -5 and variants were detd. by CD. The results indicate that all proteins have a strong tendency to adopt .alpha.-helical conformation is one of the important structural requirements for eliciting appreciable candidacidal activity. Collectively, the data suggest that in addn. to the helical conformation, specific residues such as Lys-13 and Arg-22 in the sequence of ***histatin*** -5 are, indeed, important for candidacidal activity.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 118 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:633283 CAPLUS
DN 125:316210
TI Candidacidal activity of human salivary ***histatin*** recombinant variants produced by site-directed mutagenesis
AU Driscoll, James; Duan, Chunni; Zuo, Yi; Xu, Tao; Troxler, Robert; Oppenheim, Frank G.
CS Department of Periodontology, Oral Biology, School of Graduate Dentistry, School of Medicine, Boston University Medical Center, Boston, MA, 02118, USA
SO Gene (1996), 177(1/2), 29-34 CODEN: GENED6; ISSN: 0378-1119
PB Elsevier
DT Journal
LA English
AB ***Histatin*** 5 (Hst5) is a 24-amino acid (aa) member of the Hst family that is found in human salivary secretions and exhibits candidacidal activity. Hst5 contains a 13-aa region that alone is capable of killing fungal pathogens and is referred to as the functional domain. To investigate the role of specific aa located within the functional domain, the pRSET bacterial expression system was used to produce recombinant Hst5 (re-Hst5) and several re-variants that were generated by site-directed mutagenesis. The vector pRSETC expresses genes of interest as fusion proteins attached to the carboxy end of an N-terminal His6 tag that binds to nickel (Ni2+). The re-variants were generated using the polymerase chain reaction (PCR) and had Gly substituted for either the His, Glu or Lys/Arg within the functional domain. PCR products that encoded either the wild-type or variant forms of re-Hst5 were inserted into pRSETC and produced as fusion proteins which were affinity purified from cell lysates by Ni2+-Sepharose chromatog. Fusion proteins were digested with CNBr and re-Hsts were purified by reversed-phase high performance liq. chromatog. (RP-HPLC). Re-Hsts were tested in bioassays to measure the ability to kill both Candida albicans blastoconidia and spheroplasts which were generated by removal of the cell wall. In both assays, re-Hst5 displayed dose-dependent candidacidal activity that was nearly identical to that of native Hst5 purified from human salivary secretions. Re-Hst5 variants with either Glu or Lys/Arg substitutions demonstrated significantly lower candidacidal activity in both assays, while the variant with His mutated showed essentially no activity at physiol. concns. These results indicate that acidic and basic aa within the functional domain contribute to candidacidal activity and that the His are essential for candidacidal activity. Addnl., since C. albicans spheroplasts were also susceptible to Hsts, the cell wall is not an essential component in the Hst mechanism of candidacidal action.

L3 ANSWER 119 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:572973 CAPLUS
DN 125:265062
TI Stabilization of helix by side-chain interactions in ***histatin*** -derived peptides: role in candidacidal activity
AU Ramalingam, Kalaiyarasi; Gururaja, Tarikere L.; Ramasubbu, Narayanan; Levine, Michael J.
CS Dep. Oral Biol., State Univ. New York, Buffalo, Buffalo, NY, 14214, USA
SO Biochemical and Biophysical Research Communications (1996), 225(1), 47-53 CODEN: BBRCA9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
AB Candida albicans is an opportunistic pathogen prevalent in AIDS patients and oral candidiasis. Azole-based drugs are currently used in the treatment of candidiasis. Histidine-rich peptides (***histatins***), are the natural inhibitors of Candida species present in human salivary secretions. Sequence comparison of ***histatins*** revealed the common motif -KRKFHE- in active peptide fragments. Mol. modeling anal. showed structural similarity between this segment of ***histatins*** and azole-based drugs. The helical conformation adopted by ***histatin*** -5 may be stabilized by two side chain-side chain interactions (Phe. . . His and Arg. . .Glu). Based on sequence comparison of ***histatin*** peptides and mol. modeling, a synthetic 10-residue peptide derived from ***histatin*** -5 was helical and possessed significant anti candida activity. This peptide may be used as a template to develop ***histatin*** -based drugs for treating oral candidiasis.

L3 ANSWER 120 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:522010 CAPLUS
DN 125:230573
TI Novel, burst free, programmable biodegradable microspheres for controlled release of polypeptides
AU Jeyanthi, R.; Akiyama, A.; Friden, P.; Roberts, F.D.; van Hamont, J.; Reid, R.; McQueen, C.
CS Periodontix, Inc., Watertown, MA, 02172, USA
SO Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1996), 23rd, 351-352 CODEN: PCRMEY; ISSN: 1022-0178
PB Controlled Release Society, Inc.
DT Journal
LA English
AB The use of "uncapped" lactide-glycolide copolymers in combination with the "capped" copolymer and an aq. emulsification technique to provide novel, burst-free, programmable sustained-release of polypeptides up to 100 days without the use of fillers or additives is presented. A fragment of ***histatin*** 5, a cationic salivary peptide was used as a model peptide to demonstrate this 30-100 day delivery system.

L3 ANSWER 121 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:501688 CAPLUS
DN 125:150823
TI ***Histatins*** as antimicrobial agents for cosmetics and dentifrices
IN Chikindas, Michael C. L.; Joiner, Andrew; Small, Philip W.
PA Unilever N.V., Neth.; Unilever Plc
SO Eur. Pat. Appl., 9 pp. CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- -------------- --------
PI EP 721774 A2 19960717 EP 1995-203398 19951207 EP 721774 A3 19990310 EP 721774 B1 20021002 R: CH, DE, ES, FR, GB, IT, LI, NL, SE US 5672351 A 19970930 US 1995-570182 19951211
PRAI EP 1994-309258 A 19941212
AB The present invention relates to antimicrobial cosmetic compns. for the care of the human body or parts thereof, comprising derivs. of ***histatins*** or fragments thereof. The antimicrobial activity of ***histatins*** or their fragments can be significantly enhanced by capping them at the C-terminus or at the C- and N-terminus and/or complexing them with antimicrobially-active metal ions. The modified ***histatins*** and ***histatin*** fragments have a significantly increased activity against a range of microbial strains, and are useful as controlled delivery agents for the metal ions. They are suitable for a whole range of anti-caries, anti-bad breath oral applications,

deodorant applications, personal hygiene applications and so on, for which they are included in any suitable carrier medium. Preferred are the capped derivs., which have been complexed with Ag, Cu, Zn or Sn.

L3 ANSWER 122 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:420524 CAPLUS
DN 125:110939
TI Temporal and compositional characteristics of salivary protein adsorption to hydroxyapatite
AU Lamkin, M. S.; Arancillo, A. A.; Oppenheim, F. G.
CS Medical Center, Boston University, Boston, MA, 02118, USA
SO Journal of Dental Research (1996), 75(2), 803-808 CODEN: JDREAF; ISSN: 0022-0345
PB International Association for Dental Research
DT Journal
LA English
AB Salivary proteins bind to enamel surfaces and hydroxyapatite in a highly selective manner. Numerous studies have identified these proteins as primarily proline-rich proteins, cystatins, statherin, and ***histatins*** . Previously, the hydroxyapatite-binding potential of these proteins had been characterized in systems consisting of singly purified protein and adsorbent. The purpose of this study was to investigate the adsorption of each protein in the presence of complete salivary secretion. Proteins, shown to adsorb to hydroxyapatite, were purified, biotinylated, and added back to the remaining proteins to form a series of reconstituted secretions. The adsorption of each biotinylated protein in the reconstituted secretion to hydroxyapatite was then measured as a function of time. Results indicated that 3 different adsorption patterns occur. A simple hyperbolic pattern is characteristic of amylase, glycosylated proline-rich protein (PRG), and cystatin. A faster adsorption process is obsd. for PRP-3, PRP-4, PIF-f, and statherin. A more complex pattern, exhibiting a rapid phase followed by a slower phase, is characteristic of PRP-1, PRP-2, PIF-s, and ***histatins*** . These results suggest that there are different adsorption processes involved in the binding of salivary proteins to hydroxyapatite. Two possible mechanisms are direct adsorption of protein to hydroxyapatite and indirect adsorption of protein by interacting with other proteins already bound to hydroxyapatite.

L3 ANSWER 123 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:289462 CAPLUS
DN 124:335715
TI A current research for salivary peptides, ***histatins*** : their properties and biological activities
AU Ishibashi, Kazunari; Abe, Kimio
CS Dep. Oral Biochem., Fukuoka Dental Coll., Fukuoka, 814-01, Japan
SO Fukuoka Shika Daigaku Gakkai Zasshi (1996), 23(1), 1-21 CODEN: FSDZD4; ISSN: 0385-0064
PB Fukuoka Shika Daigaku Gakkai
DT Journal; General Review
LA Japanese
AB A review with 115 refs. on the structure, polymorphism, cellular location, and function of ***histatins*** .

L3 ANSWER 124 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:267015 CAPLUS
DN 124:315232
TI Industry perspectives on the use of natural antimicrobials and inhibitors for food applications
AU Gould, Grahame W.
CS Unilever Research Laboratory, Sharnbrook/Bedford, MK44 ILQ, UK
SO Journal of Food Protection (1996), (Suppl.), 82-6 CODEN: JFPRDR; ISSN: 0362-028X
PB International Association of Milk, Food and Environmental Sanitarians
DT Journal; General Review
LA English
AB A review with 54 refs. The wide range of extremely effective naturally occurring antimicrobial systems include those derived from animals (e.g., enzymes such as lysozyme and lactoperoxidase; other proteins such as lactoferrin, lactoferricin, ovotransferrin, and serum transferrins; small peptides such as ***histatins*** and magainins; and the immune system), those derived from plants (e.g., phytoalexins, low-mol.-wt. components of herbs and spices; phenolics such as oleuropein; and essential oils) and those derived from microorganisms (e.g., bacteriocins such as nisin and pediocin). An increasing no. of such natural systems is being deliberately utilized for food preservation, or being explored for such use. The future potential is substantial, particularly as the efficacy of these systems is demonstrated in additive or synergistic combinations with some of the other antimicrobial factors that we can employ to improve the safety and shelf stability of foods. While "naturalness" alone is not necessarily a sufficient objective for these developments, the use of natural inhibitors as components of systems that can together enhance the effectiveness of preservation, with advantages in product quality and safety, justifies pursuit.

L3 ANSWER 125 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:249668 CAPLUS
DN 124:336096
TI Functional comparison of native and recombinant human salivary ***histatin*** 1
AU Driscoll, J.; Zuo, Y.; Xu, T.; Choi, J.R.; Troxler, R.F.; Oppenheim, F.G.
CS School of Graduate Dentistry, Boston University, Boston, MA, 02118, USA
SO Journal of Dental Research (1995), 74(12), 1837-44 CODEN: JDREAF; ISSN: 0022-0345
PB International Association for Dental Research
DT Journal
LA English
AB ***Histatin*** 1 is a histidine-rich phosphoprotein present in human parotid saliva that possesses candidacidal activity and functions in mineralization by adsorbing to hydroxyapatite. The objective of the present study was to develop a system for recombinant prodn. of ***histatin*** 1 and to examine the role of phosphorylation in the functional activities of this mol. Native ***histatin*** 1 (contg. a phosphoserine at residue 2) was purified from parotid saliva, whereas a bacterial expression system was used to produce a recombinant form of ***histatin*** 1 (re-Hst1) that lacked phosphorylated serine. ***Histatin*** 1 cDNA was inserted into the vector pGEX-3X, which expresses foreign genes as sol. fusion proteins attached to the carboxyl-terminus of glutathione S-transferase (GST). The GST/re-Hst1 fusion protein was isolated from cell lysates by affinity chromatog. on glutathione (GSH)-Sepharose and digested with cyanogen bromide to sep. re-Hst1 from the GST fusion partner. The digest was subjected to reversed-phase high-performance liq. chromatog. on a C18 column, and re-Hst1 was eluted as a well-defined peak. The yield of re-Hst1 was 4 mg/L of bacterial culture. Amino-terminal sequencing and amino acid anal. confirmed the final product as re-Hst1. SDS-PAGE showed that native ***histatin*** 1 and re-Hst1 had the same apparent mol. wts., while cationic PAGE showed that re-Hst1 was more basic. Phosphate anal. indicated 1 mol phosphate/mol of native ***histatin*** 1, while re-Hst1 lacked any detectable phosphate. Re-Hst1 demonstrated candidacidal activity comparable to that of

native ***histatin*** 1, but displayed substantially lower binding to hydroxyapatite. These results show that phosphorylation of ***histatin*** 1 at residue 2 contributes significantly to its ability to bind to hydroxyapatite.

L3 ANSWER 126 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:137935 CAPLUS
DN 124:220489
TI ***Histatin*** fragments for use as antifungals
IN Oppenheim, Frank G.; Xu, Tao
PA The Trustees of Boston University, USA
SO U.S., 19 pp. Cont. of U.S. Ser. No. 145,030, abandoned. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 7 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI US 5486503 A 19960123 US 1994-287717 19940809 US 5696078 A 19971209 US 1995-441914 19950516 US 5631228 A 19970520 US 1995-481888 19950607 US 5646119 A 19970708 US 1995-485273 19950607 US 5912230 A 19990615 US 1998-973559 19980311 US 5885965 A 19990323 US 1998-973563 19980312
PRAI US 1991-786571 B1 19911101 US 1993-145030 B1 19931028 US 1994-287717 A3 19940809 US 1995-481888 A2 19950607 US 1995-485273 A2 19950607 WO 1996-US9374 W 19960607 WO 1996-US9962 W 19960607
AB Peptides representing defined portions of the amino acid sequences of naturally occurring human and macaque ***histatins*** , modified peptides, expression vectors encoding these peptides, and compns. and methods for treatment of fungal infection are described. Some of the ***histatin*** -based peptides exhibit superior anti-fungal activity to native, intact ***histatins*** . Isolated, naturally occurring macaque ***histatins*** and peptide analogs are also described.

L3 ANSWER 127 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:81591 CAPLUS
DN 124:127138
TI Glucan-binding proteins, especially glycosyltransferase, and use of fusion proteins to prevent dental plaque and teeth staining
IN Kuramitsu, Howard Kikuo; Schilling, Kurt Matthew
PA Unilever NV, Neth.; Unilever PLC
SO PCT Int. Appl., 44 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI WO 9531556 A1 19951123 WO 1995-GB1070 19950511 W: JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE EP 759081 A1 19970226 EP 1995-918091 19950511 R: DE, FR, GB, IT JP 10500127 T2 19980106 JP 1995-529437 19950511
PRAI GB 1994-9387 19940511 WO 1995-GB1070 19950511
AB Polypeptides with specific binding affinity for glucan - esp. the glucan-binding domain of glycosyl transferase enzyme - is utilized in a compn. for oral care. The polypeptide may block the binding sites in dental plaque where glycosyl transferase would bind and generate more plaque, or it may be conjugated to - and provide targeted delivery of - an antiplaque or antistain agent.

L3 ANSWER 128 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:969749 CAPLUS
DN 123:350366
TI Pharmaceutical compositions containing cell growth factor and ***histatin*** for bone disease
IN Taniguchi, Shinjiro; Takemura, Akane; Matsuda, Naoki; Tsunemitsu, Akira
PA Sunstar Kk, Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI JP 07258110 A2 19951009 JP 1994-76628 19940322
PRAI JP 1994-76628 19940322
AB Pharmaceutical compns. for bone disease (such fracture) contain epidermal growth factor and ***histatin*** , preferably ***histatin*** -5. An injection contained epidermal growth factor 1, ***histatin*** -5 200, NaCl 900mg and injection water to 100mL. The prepns. were effective and stable.

L3 ANSWER 129 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:859964 CAPLUS
DN 123:248836
TI Identification of ***histatins*** as tannin-binding proteins in human saliva
AU Yan, Qingyou; Bennick, Anders
CS Dep. Biochem., Univ. Toronto, Toronto, ON, M5P 1A8, Can.
SO Biochemical Journal (1995), 311(1), 341-7 CODEN: BIJOAK; ISSN: 0264-6021
PB Portland Press
DT Journal
LA English
AB To identify tannin-binding human salivary proteins, parotid and submandibular/sublingual saliva samples were adsorbed with tannin. Proline-rich proteins (PRPs), and in particular a group of low-Mr proteins, were readily pptd. by tannin. The low-Mr proteins were purified from parotid saliva and demonstrated to be ***histatins*** , a family of well-characterized histidine-rich salivary proteins. The ability of synthetic ***histatin*** 5, as well as an acidic PRP (PRP-1) and gelatin to ppt. quebracho condensed tannin and tannic acid was detd. At pH 7.4 ***histatin*** 5 was the most effective precipitant of both condensed tannin and tannic acid and it also pptd. the largest amt. of condensed tannin at pH 3.0, but the smallest amt. of tannic acid at that pH. In contrast PRP-1 showed a greater ability to ppt. both condensed tannin and tannic acid at pH 3.0 than at pH 7.4. Under most circumstances ***histatin*** 5 was therefore more effective in pptg. tannins than proteins with high proline content which generally have been recognized as strong precipitants of tannin. Pre-incubation of tannic acid with .alpha.-amylase inhibited the enzyme, but addn. of ***histatin*** 5 or the acidic PRP PIF-s protected amylase from inhibition by tannin. Similarly salivary proteins may protect other biol. activities in the digestive tract from inhibition by dietary tannin.

L3 ANSWER 130 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:836287 CAPLUS
DN 123:237764
TI Surface-modified poly(methyl methacrylate) enhances adsorption and retains anticandidal activities of salivary ***histatin*** 5
AU Edgerton, M.; Raj, P. A.; Levine, M. J.
CS Dep. of Oral Biology and Dental Research Inst., State Univ. of New York at Buffalo, Buffalo, NY, 14214, USA
SO Journal of Biomedical Materials Research (1995), 29(10), 1277-86 CODEN: JBMRBG; ISSN: 0021-9304
PB Wiley
DT Journal
LA English
AB Denture-induced stomatitis is a common intraoral disease which is assocd. with high levels of Candida albicans adhesion to denture surface. The aim of this study was to produce a surface-modified denture resin, which is usually manufd. from poly(Me

methacrylate) (PMMA), carrying an immobilized anticandidal protein. PMMA was modified by surface polymn. of Me methacrylic acid to enhance adsorption of a potent candidacidal salivary protein, human ***histatin*** 5. The modified PMMA showed higher surface adsorption and desorption of ***histatin*** 5 than the unmodified material. Because ***histatin*** 5 destabilizes C. albicans cell membranes and allows efflux of intracellular mols., candidacidal activity was monitored by dye release from fungal cells. Adsorbed ***histatin*** 5 did not release dye from the yeast cells; however, dye was detected as ***histatin*** was desorbed from the surface. In an adhesion assay, modified PMMA decreased human submandibular-sublingual saliva (HSMSL) mediated adherence of yeast cells to the polymer. Precoating ***histatin*** 5 onto unmodified PMMA also abolished HSMSL-mediated adhesion. These expts. show that dental acrylic may be surface modified and loaded with ***histatin*** 5 as a means of controlled release of ***histatin*** 5 to an affected area. This surface modification may addnl. reduce adhesion of C. albicans cells to the saliva-coated material.

L3 ANSWER 131 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:802765 CAPLUS
DN 123:331185
TI Recombinant ***histatins*** : functional domain duplication enhances candidacidal activity
AU Zuo, Yi; Xu, Tao; Troxler, Robert F.; Li, James; Driscoll, James; Oppenheim, Frank G.
CS Department of Periodontology and Oral Biology, School of Graduate Dentistry, Boston University Medical Center, Boston, MA, 02118, USA
SO Gene (1995), 161(1), 87-91 CODEN: GENED6; ISSN: 0378-1119
PB Elsevier
DT Journal
LA English
AB ***Histatin*** 3 (Hst3) is a 32-amino-acid (aa) His-rich protein with antimicrobial activity found in human salivary secretions. To explore further the structure/function relationship of Hst, we utilized a bacterial system for the efficient prodn. of recombinant Hst3 (re-Hst3) and Hst variants. Previously, we demonstrated that the middle portion of Hst3 (aa 13-24) contains the functional domain responsible for killing Candida albicans. Using PCR and splice overlap extension, a Hst variant (re-Hst3rep) was made in which the functional domain was repeated in tandem. Using the pRSET bacterial expression system, re-Hst3 and the variant re-Hst3rep were produced as chimeric fusions and were isolated from bacterial sonicates by affinity chromatog. Affinity purified fusion proteins were digested with CNBr and re-Hst were sepd. from their fusion partners by reverse-phase high-performance liq. chromatog. The activity of re-Hst3 and re-Hst3rep was compared to that of native Hst3 from human salivary secretions in the C. albicans killing assay. The LD50 values for candidacidal activity of native Hst3, re-Hst3 and re-Hst3rep were 7.2, 6.8 and 4.1 nmol/mL, resp. At lower concns. re-Hst3rep was five times more active than native Hst3 or re-Hst3 and at even lower concns. re-Hst3rep exhibited significant candidacidal activity while native Hst3 and re-Hst3 were inactive. These results demonstrate an expression system for prodn. of biol. active functional Hst and Hst variants and shows that repetition of the functional domain of Hst3 enhances candidacidal activity.

L3 ANSWER 132 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:705848 CAPLUS
DN 123:140962
TI Immunology for dentist. IX. Immunology of oral diseases
AU Okuda, Katsuji
CS Dep. Microbiol., Tokyo Dent. Coll., Chiba, 261, Japan
SO Shika Gakuho (1995), 95(5), 439-48 CODEN: SHGKA3; ISSN: 0037-3710
DT Journal; General Review
LA Japanese
AB A review with 8 refs., on the function of salivary secretory IgA, non-specific antimicrobial substances such as mucin, lysozyme, lactoferrin, peroxidase, and ***histatin*** in saliva, gingival crevicular fluid, and immunopathol. of periodontal diseases and oral ulcers.

L3 ANSWER 133 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:566365 CAPLUS
DN 123:6858
TI Immunoreactive ***histatin*** 5 in salivary gland tumors
AU Shrestha, Prashanta; Hashimoto, Junji; Takagi, Hisashi; Yamada, Kazuto; Mori, Masahiko; Kanehira, Takashi; Wang, Paoli; Kuboki, Yoshinori
CS Departments Oral and Maxillofacial Surgery, Asahi University School Dentistry, Gifu, 501-02, Japan
SO Acta Histochemica et Cytochemica (1994), 27(6), 527-34 CODEN: ACHCBO; ISSN: 0044-5991
PB Japan Society of Histochemistry and Cytochemistry
DT Journal
LA English
AB ***Histatins*** are a group of histidine-rich polypeptides specific to parotid and submandibular gland secretions with several different biol. functions such as stabilization of mineral-solute interaction in oral fluids, and antibacterial and antifungal actions. The authors generated polyclonal antibody to ***histatin*** by using purified ***histatin*** 5 as an immunogen and assayed the immunoreactivity by ELISA and immunoblotting. The antibody was further used to localize ***histatin*** in normal glands and tumors of salivary glands, pleomorphic adenoma, Warthin's tumor, adenoid cystic, acinic cell, mucoepidermoid, papillary cystadenocarcinoma and undifferentiated carcinoma by immunohistochem. methods. The normal major and minor human salivary glands showed an intense immunoreactivity in ductal cells, trace immunoreactivity in serous acini, and no immunoreactivity in mucous acinar cells, suggesting ***histatin*** is mainly produced by ductal cells and to a lesser extent by serous cells. A consistent immunoreactivity of ***histatin*** in ductal segments of normal glands and a variable expression in the tumor cells of all the neoplastic lesions examd. may implicate a role of this polypeptide in normal salivary gland function and salivary tumors. In addn., the findings may implicate common precursor cells, however, differing in the state of differentiation in normal and neoplastic conditions.

L3 ANSWER 134 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:533565 CAPLUS
DN 123:6440
TI Characterization of low-molecular-weight peptides in human parotid saliva
AU Perinpanayagam, H. E. R.; Wuyckhuyse, B. C. Van; Ji, Z. S.; Tabak, L. A.
CS Departments Dental Research and Biochemistry, University Rochester, Rochester, NY, 14642, USA
SO Journal of Dental Research (1995), 74(1), 345-50 CODEN: JDREAF; ISSN: 0022-0345
DT Journal
LA English
AB The low-mol.-wt. components of human saliva remain poorly characterized. Therefore, low-mol.-wt. peptides (Mr<3000) have been purified from human parotid saliva and characterized with respect to their amino acid sequence. From the sequences

obtained, it is likely that these peptides are derived from proteolysis of the hydroxyapatite-interactive human salivary proteins, ***histatins*** , proline-rich proteins, and statherins. Since human parotid saliva is an amicrobial fluid, much of the low-mol.-wt. peptide fraction of this secretion appears to be derived from the proteolytic processing of the larger proteins. Because of their small size, these peptides are likely to be in exchange with dental plaque fluid and may therefore help modulate events such as demineralization/remineralization, microbial attachment, and dental plaque metab. at the tooth-saliva interface.

L3 ANSWER 135 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:387215 CAPLUS
DN 122:184005
TI Physiological regulation of the secretion of ***histatins*** and statherins in human parotid saliva
AU Jensen, J.L.; Xu, T.; Lamkin, M.S.; Brodin, P.; Aars, H.; Berg, T.; Oppenheim, F.G.
CS School of Graduate Dentistry, Boston University, Boston, MS, USA
SO Journal of Dental Research (1994), 73(12), 1811-17 CODEN: JDREAF; ISSN: 0022-0345
DT Journal
LA English
AB The small salivary phosphoproteins, ***histatins*** and statherins, have important functions in the oral cavity in terms of antimicrobial actions and regulation of calcium phosphate homeostasis. Neither the effects of various physiol. stimuli on their secretion nor the nature of the efferent receptor involved in the stimulus-secretion coupling has been detd. previously. These aspects are important for improved understanding of the secretory control of salivary proteins and may have implications regarding the effects of specific medications on salivary constituents and oral health. The effects of graded mech. (chewing on short and long silicone tubings) and gustatory stimulation (0.5, 1.5, and 5.0% citric acid) on the secretion of ***histatins*** and statherins were studied in the presence and absence of adrenolytic agents (n = 10). In this model, secretory rates of both proteins increased with increases in flow rate, with 5.0% citric acid representing a particularly potent stimulus. ***Histatin*** and statherin secretory rates were significantly reduced by the .beta.1-adrenolytic agent (***histatins*** to 58 to 72% and statherins to 11 to 29% of that in corresponding control expts.), but not by the .alpha.1-adrenolytic agent. Since the .beta.1-adrenergic receptors played an important role in the stimulus-secretion coupling of these proteins, protective salivary functions in the oral cavity may be compromised during .beta.1-adrenolytic treatment.

L3 ANSWER 136 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:300216 CAPLUS
DN 122:89439
TI Topical preparations containing peptides for wound healing promotion
IN Matsuda, Naoki; Takemura, Akane; Taniguchi, Shinjiro
PA Sunstar Kk, Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI JP 06287146 A2 19941011 JP 1993-98530 19930331
PRAI JP 1993-98530 19930331
AB Topical prepns. contain peptides with 3-34 amino acid residues having directly linked with .gtoreq.2 basic amino acid residues. A gel contg. Lys-His-His-Ser-His-Arg-Gly-Tyr was applied to injured rats to accelerate wound healing. Gly-His-Lys 1.0, hydroxyethyl cellulose 4.0, triacetin 12.0, Eudragit RS 2.0, and glycerin to 100 wt.% were mixed to give a gel.

L3 ANSWER 137 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:65158 CAPLUS
DN 122:78129
TI Two coding change mutations in the HIS22 allele characterize the salivary ***histatin*** 3-2 protein variant
AU Sabatini, Linda M.; Azen, Edwin A.
CS Department Pathology and Laboratory Medicine, University Wisconsin, Madison, WI, 53792, USA
SO Human Mutation (1994), 4(1), 12-19 CODEN: HUMUE3; ISSN: 1059-7794
DT Journal
LA English
AB The decoded amino acid sequence of a salivary protein variant, ***histatin*** 3-2 (formerly termed Pb c), that is found primarily and in high frequency in Black populations was detd. by genomic PCR and direct sequencing of the HIS22 allele. Two different mutations that cause coding changes were found in exon 5. The first mutation is a single nucleotide (T .fwdarw. A) substitution that causes a TAT (Tyr) .fwdarw. TAA (Stop) change at residue 28. This premature stop mutation results in a 27 amino acid ***histatin*** 3-2 protein, which is 5 amino acids smaller than the common ***histatin*** 3-1 allelic protein (a product of the HIS21 allele). The second mutation, a single nucleotide (G .fwdarw. A) substitution (located only 19 nucleotides upstream of the first mutation) causes a CGA (Arg) .fwdarw. CAA (Gln) change at residue 22, which eliminates a proteolytic cleavage site. These two mutations explain the differences in electrophoretic patterns of HIS21 vs. HIS22 coded ***histatin*** peptides and may have functional significance. Each mutation alters a different DNA restriction site, and this provides a DNA-based test for the mutations. This test should greatly simplify population and family studies of this protein polymorphism, since the saliva-based test is considerably more problematic. Elucidation here of the derived protein sequence of the variant ***histatin*** 3-2 protein may also facilitate functional studies.

L3 ANSWER 138 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:30372 CAPLUS
DN 122:181165
TI Isolation and amino acid sequences of oligopeptides from human parotid saliva
AU Tsubura, Shuichi; Sanada, Kazuo
CS Sch. Dent. Niigata, Nippon Dent. Univ., Niigata, 951, Japan
SO Shigaku (1994), 82(1), 138-52 CODEN: SHIGAZ; ISSN: 0029-8484
DT Journal
LA Japanese
AB The chem., phys., and genetic characteristics of proteins and peptides in human saliva have been studied by several investigators. However, only a few observations on the chem. structure of oligopeptides in saliva have been reported. In the present study, the authors have detd. the amino acid sequences of 14 oligopeptides of human parotid saliva by the DNS-Edman method. The results obtained were as follows. (1) An improved method for isolation and purifn. of salivary oligopeptides was investigated. The low mol. peptides in the 80% methanol sol. fraction were divided into 4 fractions using a Bio-Gel P-4 column, and the oligopeptide-contg. fractions were obtained by cation exchange chromatog. The amino acid sequences of 14 oligopeptides were detd. The sequences of two of the oligopeptides appear to correspond to N-terminal residues from the basic proline-rich-peptide P-D. Another oligopeptide is

identical to the C-terminal 5 residues of the histidine-rich protein, ***histatin*** -1 .apprx. 4.

L3 ANSWER 139 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:708303 CAPLUS
DN 121:308303
TI Regeneration accelerators for periodontal tissue and the materials
IN Takemura, Akane; Matsuda, Naoki; Taniguchi, Shinjiro
PA Sunstar Kk, Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- -------------- --------
PI JP 06234653 A2 19940823 JP 1993-45998 19930210
PRAI JP 1993-45998 19930210
AB The title accelerators and their materials (e.g. paper strip) contain peptides having 3-34 amino acid residues and sequences of .gtoreq.2 consecutive basic amino acids in a row. Lys-His-His-Ser-His-Arg-Gly-Tyr at 0.1 mg/mL strongly enhanced the growth of periodontal fibroblast cell and the activity was synergetically enhanced with the concomitant use of epidermal growth factor. Some formulation data are given.

L3 ANSWER 140 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:479049 CAPLUS
DN 121:79049
TI Macromolecular inhibitors of crystallization in bile and saliva
AU Verdier, Jean-Michel
CS Unite de Rech. et Pathol. Dig., INSERM U315, Marseille, Fr.
SO Nephrologie (1993), 14(6), 251-5 CODEN: NEPHDY; ISSN: 0250-4960
DT Journal; General Review
LA French
AB A review, with 20 refs., on the current knowledges concerning macromol. inhibitors of crystn. in saliva and in bile, including the the statherins, the acidic proline-rich proteins, the cystatins and the ***histatins*** in saliva and the apolipoproteins and the calcium-binding protein also called anionic polypeptide fraction in bile. The structure-function relationships of these mols. are particularly stressed.

L3 ANSWER 141 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:317997 CAPLUS
DN 120:317997
TI Membrane-induced helical conformation of an active candidacidal fragment of salivary ***histatins***
AU Raj, Periathamby Antony; Soni, Sunil Datta; Levine, Michael J.
CS Dep. Oral Biol., State Univ. New York, Buffalo, NY, 14214, USA
SO Journal of Biological Chemistry (1994), 269(13), 9610-19 CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB The conformational preference of the candidacidal C-terminal 16-residue fragment (9-24; GYKRKFHEKHHSHRGY) of salivary ***histatin*** 5 was examd. in H2O, MeOH, and DMSO solns. using 500 MHz 2-dimensional-NMR. Fourier transform IR and CD spectroscopy were used to delineate its membrane-bound conformation in lipid vesicles. The peptide backbone and side-chain proton resonance assignments were accomplished by 2-dimensional total correlated and nuclear Overhauser effect (NOE) spectra. The coupling const. (JNH-C.alpha.H) values detd. from the double quantum-filtered correlated spectra, temp. coeffs. of NH chem. shifts (d.delta./dT), 1H/2H exchange rates on amide resonances, and the set of NOE connectivities were used to delineate backbone conformational features. The high JNH-C.alpha.H values (.gtoreq.7.4 Hz), absence of any characteristic NH-NH (i, i+1) or C.alpha.H-C.beta.H (i,i+3) NOE connectivities, high d.delta./dT values (.gtoreq.0.004), and the fast 1H/2H amide exchange suggest that the ***histatin*** peptide favors unfolded random conformations in aq. soln. at pH 3.8. In contrast, the JNH-C.alpha.H values (.ltoreq.6.5 Hz), slow 1H/2H exchange, low d.delta./dT values (.ltoreq.0.003) obsd. for amide resonances of residues 5-16, and the characteristic NH-NH (i,i+1), C.alpha.H-C.beta.H (i,i+3) NOE connectivities, provide evidence for the presence of largely .alpha.-helical conformations in DMSO, which mimics the polar aprotic membrane environment. In methanolic solns., 310-helical conformations could exist as a minor population together with the major .alpha.-helical conformations. Fourier transform IR spectroscopy and CD data indicate that lipid environments such as dimyristoylphosphatidylcholine vesicles could induce the peptide to fold into predominantly .alpha.-helical conformation. The results suggest that in DMSO and dimyristoylphosphatidylcholine vesicles the candidacidal domain of salivary ***histatin*** 5 prefers a largely helical conformation, which could facilitate its interaction with the membrane of Candida albicans. The mechanism of antimicrobial action of this class of polypeptides appears to involve primarily electrostatic and hydrogen-bonding interaction of cationic and polar residues with the head groups of the plasma membranes of target cells.

L3 ANSWER 142 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:295211 CAPLUS
DN 120:295211
TI The influence of ***histatin*** -5 fragments on the mineralization of hydroxyapatite
AU Richardson, C. F.; Johnsson, M.; Raj, P. A.; Levine, M. J.; Nancollas, G. H.
CS Dep. Chem., State Univ. New York, Buffalo, NY, 14214, USA
SO Archives of Oral Biology (1993), 38(11), 997-1002 CODEN: AOBIAR; ISSN: 0003-9969
DT Journal
LA English
AB The adsorption of ***histatin*** 5 on hydroxyapatite (HAP) was detd. and compared to that of several fragments of ***histatin*** 5, such as residues 1-16 (N16), 7-16 (M10), 9-24 (C16), 11-24 (C14), 13-24 (C12), 15-24 (C10). The influence of the adsorbed peptides on the seeded crystal growth of HAP was investigated with the const. compn. method. The adsorption affinity of the peptides as well as their ability to inhibit mineralization was influenced by the length of the peptide chain. ***Histatin*** 5 showed the highest affinity, as detd. by a Langmuir model, whereas the smaller C10 and C12 displayed the lowest equil. uptake. The smaller C10 and C12 peptides were, on the other hand, more effective as crystal growth inhibitors, indicating a more efficient coverage of surface active sites. Electrophoretic mobility data indicated an increase in the pos. charge at the HAP surface in the presence of these peptides, which were efficient HAP crystallite dispersants.

L3 ANSWER 143 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:104910 CAPLUS
DN 120:104910
TI Anti-lipopolysaccharide activity of ***histatins*** , peptides from human saliva
AU Sugiyama, K.
CS Dent. Sch., Okayama Univ., Okayama, 700, Japan
SO Experientia (1993), 49(12), 1095-7 CODEN: EXPEAM; ISSN: 0014-4754
DT Journal
LA English

AB ***Histatins*** are histidine-rich polypeptides secreted in human saliva. They were found to inhibit lipopolysaccharide (LPS)-mediated gelation of Limulus amoebocyte lysate, and to reverse the anti-complement action of LPS or lipid A. ***Histatins*** also gave ppt. bands in agarose gels with various LPS. The results indicate that ***histatins*** neutralized the activity of LPS by binding to the lipid A moiety of LPS.

L3 ANSWER 144 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:97176 CAPLUS
DN 120:97176
TI ***Histatin*** as a synergistic stimulator with epidermal growth factor of rabbit chondrocyte proliferation
AU Murakami, Yukitaka; Nagata, Hideki; Shizukuishi, Satoshi; Nakashima, Kazuhisa; Okawa, Tokutaro; Takigawa, Masaharu; Tsunemitsu, Akira
CS Fac. Dent., Osaka Univ., Osaka, Japan
SO Biochemical and Biophysical Research Communications (1994), 198(1), 274-80 CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB ***Histatin*** 5 dose-dependently increased DNA synthesis in rabbit costal chondrocytes in culture. The level of DNA synthesis stimulated by ***histatin*** 5 was about 4-fold that of control. The combination of ***histatin*** 5 and EGF increased DNA synthesis to about 40-fold that of control while EGF alone stimulated it 15-fold, indicating synergistic stimulation by both factors. ELISA using anti- ***histatin*** 5 demonstrated that human serum contained ***histatin*** -like substances. These findings suggest that ***histatins*** play an important role in chondrocyte proliferation, presumably as a physiol. modulator of the action of EGF.

L3 ANSWER 145 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:94725 CAPLUS
DN 120:94725
TI Role of an arginine residue present in ***histatin*** 8 which inhibits coaggregation between Porphyromonas gingivalis and Streptococcus mitis
AU Murakami, Yukitaka; Nagata, Hideki; Shizukuishi, Satoshi; Tsunemitsu, Akira
CS Fac. Dent., Osaka Univ., Suita, 565, Japan
SO Koku Eisei Gakkai Zasshi (1993), 43(2), 221-3 CODEN: KEGZA7; ISSN: 0023-2831
DT Journal
LA Japanese
AB Inhibitory effects of the five synthetic peptides from ***histatin*** 8 with and without an arginine residue were examd. on coaggregation between P. gingivalis and S. mitis. Coaggregation was strongly inhibited by peptides Lys-Phe-His-Glu-Lys-His-His-Ser-His-Arg-Gly-Tyr and Lys-Phe-His-Glu-Lys-His-His-Ser-His-Arg, moderately by peptides Lys-His-His-Ser-His-Arg-Gly-Tyr and Lys-His-His-Ser-His-Arg, and far less by peptide Lys-His-His-Ser-His. These results suggested that the arginine residue in ***histatin*** 8 might have an important role in the inhibition of coaggregation.

L3 ANSWER 146 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:49215 CAPLUS
DN 120:49215
TI High-performance liquid chromatographic determination of ***histatins*** in human saliva
AU Sugiyama, K.; Ogata, K.
CS Dent. Sch., Okayama Univ., Okayama, 700, Japan
SO Journal of Chromatography, Biomedical Applications (1993), 619(2), 306-9 CODEN: JCBADL; ISSN: 0378-4347
DT Journal
LA English
AB The ***histatins*** in human saliva were extd. with 0.1 M HCl-methanol, and ***histatins*** 1, 3, 5 and 6 were sepd. and concns. were detd. by reversed-phase chromatog. This simple method enabled the detn. of levels of individual ***histatins*** from the saliva of normal subjects. The av. concn. of ***histatins*** 1, 3, 5, and 6 in parotid saliva collected from 26 healthy volunteers aged from 20 to 30 yr were 11.25 .+-. 5.65, 8.15 .+-. 3.08, 7.67 .+-. 3.12, and 1.56 .+-. 0.53 .mu.mol/L (mean .+-. S.D.), resp.

L3 ANSWER 147 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:619713 CAPLUS
DN 119:219713
TI Salivary proteolysis of histidine-rich polypeptides and the antifungal activity of peptide degradation products
AU Xu, L.; Lal, K.; Santarpia, R. P., III; Pollock, J. J.
CS Dep. Oral Biol. Pathol., State Univ. New York, Stony Brook, NY, 11794-8702, USA
SO Archives of Oral Biology (1993), 38(4), 277-83 CODEN: AOBIAR; ISSN: 0003-9969
DT Journal
LA English
AB Incubation of purified synthetic histidine-rich polypeptides, HRP-2, -3, -4, -5, -6 (***histatins***), with dild. human parotid saliva yielded a series of peptide degrdn. products whose structures could be detd. by gas-phase sequencing of cationic polyacrylamide gel electroblots. Sequencing indicated that two and sometimes three peptides were present in the same Coomassie blue-stained band. By comparing different individuals' salivas it was obsd. that structural variation occurs, perhaps due to differences in the concns. or specific activities of salivary proteases. Based on the structural data, four proteolytic enzyme activities are proposed. A trypsin-like and chymotrypsin-like enzymic activity(s) appear to represent the most active salivary protease; however, both an alanine-lysine endopeptidase and a histidine peptidase activity are also present in parotid saliva. In comparison to HRP-4 or HRP-6, degraded products were less active as antifungal agents against Candida albicans both in blastospore and germ-tube assays.

L3 ANSWER 148 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:554295 CAPLUS
DN 119:154295
TI The influence of molecular structure on apatite adsorption
AU Johnsson, Mats S.A.; Raj, P. A.; Levine, M. J.; Nancollas, G. H.
CS Dep. Biomater. Oral Biol., SUNY, Buffalo, NY, 14214, USA
SO Materials Research Society Symposium Proceedings (1992), 252(Tissue-Inducing Biomaterials), 55-60 CODEN: MRSPDH; ISSN: 0272-9172
DT Journal
LA English
AB The hydroxyapatite (HAP) adsorption of salivary statherin, cystatins, proline-rich proteins and ***histatins*** has been compared to the influence of these mols. on HAP crystn. in supersatd. soln. This may yield, in many cases, information about protein conformation in the adsorbed state. The results of studies involving both parent mols. and their fragments, indicated that statherin binds to HAP primarily with a 2-5 residue segment in the N-terminal part while the cystatins and proline-rich proteins bind through a segment 2-3 times larger.

L3 ANSWER 149 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:510331 CAPLUS
DN 119:110331

TI Nucleotide sequence analysis of the human salivary protein genes HIS1 and HIS2, and evolution of the STATH/HIS gene family
AU Sabatini, Linda M.; Ota, Tatsuya; Azen, Edwin A.
CS Dep. Pathol., Pennsylvania State Univ., PA, USA
SO Molecular Biology and Evolution (1993), 10(3), 497-511 CODEN: MBEVEO; ISSN: 0737-4038
DT Journal
LA English
AB Human ***histatins*** are a family of low-Mr, neutral to very basic, histidine-rich salivary polypeptides. They probably function as part of the nonimmune host defense system in the oral cavity. A 39-kb region of DNA contg. the HIS1 and HIS2 genes was isolated from 2 human genomic phage libraries as a series of overlapping clones. The nucleotide sequences of the HIS1 gene and part of the HIS21 gene were detd. The transcribed region of HIS1 spans 8.5 kb and contains 6 exons and 5 introns. The HIS1 and HIS21 genes exhibit 89% overall sequence identity, with exon sequences exhibiting 95% identity. The 2 loci probably arose by a gene duplication event .apprx.15-30 million years ago. The HIS1 sequence data were also compared with that of STATH. Human statherin is a low-Mr acidic phosphoprotein that acts as an inhibitor of pptn. of calcium phosphate salts in the oral cavity. The HIS1 and STATH genes show nearly identical overall gene structures. The HIS1 and STATH loci exhibit 77-81% sequence identity in intron DNA and 80-88% sequence identity in noncoding exons but only 38-43% sequence identity in the protein-coding regions of exons 4 and 5. These unusual data suggest that HIS1, HIS2, and STATH belong to a single gene family exhibiting accelerated evolution between the HIS and STATH coding sequences.

L3 ANSWER 150 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:250495 CAPLUS
DN 118:250495
TI sequence analysis and characterization of the Porphyromonas gingivalis prtC gene, which expresses a novel collagenase activity
AU Kato, Tetsuo; Takahashi, Nobuyoshi; Kuramitsu, Howard K.
CS Health Sci. Cent., Univ. Texas, San Antonio, TX, 78284, USA
SO Journal of Bacteriology (1992), 174(12), 3889-95 CODEN: JOBAAY; ISSN: 0021-9193
DT Journal
LA English
AB In order to examine the potential role of bacterial collagenases in periodontal tissue destruction, gene prtC was recently isolated from Porphyromonas gingivalis ATCC 53977, which expressed collagenase activity (Takahashi, N. et al., 1991). The nucleotide sequence of the gene has been detd., and the deduced amino acid sequence corresponds to a basic protein of 37.8 kDa. In addn., Southern blot anal. indicated that the prtC gene is conserved among the three major serotypes of P. gingivalis. The enzyme has been purified to near homogeneity from Escherichia coli clone NTS1 following Mono Q anion exchange and sequential gel filtration chromatog. The mol. mass of the purified enzyme was estd. by SDS-PAGE to be .apprx.35 kDa, and the active enzyme behaved as a dimer following gel filtration chromatog. The collagenase degraded sol. and reconstituted fibrillar type I collagen, heat-denatured type I collagen, and azocoll but not gelatin or the synthetic collagenase substrate 4- phenylazobenzyloxycarbonyl-Pro-Leu-Gly-Pro-d-Arg. Enzyme activity was enhanced by Ca2+ and inhibited by EDTA, sulfhydryl-blocking agents, and the salivary peptide ***histatin*** . Preliminary evidence for the existence of a second collagenase expressed by strain 53977 was also obtained.

L3 ANSWER 151 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:229795 CAPLUS
DN 118:229795
TI Identification and characterization of ***histatin*** 8 receptors on Porphyromonas gingivalis cell surfaces
AU Murakami, Yukitaka; Shizukuishi, Satoshi; Tsunemitsu, Akira; Nakashima, Kazuhisa; Kato, Yukio; Aimoto, Saburo
CS Fac. Dent., Osaka Univ., Suita, 565, Japan
SO Koku Eisei Gakkai Zasshi (1992), 42(5), 689-95 CODEN: KEGZA7; ISSN: 0023-2831
DT Journal
LA Japanese
AB The binding of ***histatin*** 8 to P. gingivalis cells was rapid, reversible, saturable, and specific. The apparent Kd was 3.9 .times. 10-6M indicating a low affinity and, the no. of binding sites per cell was 1.5 .times. 104. These values were estd. in the absence of Cu2+ in the binding assay system. The addn. of Cu2+ to the reaction mixt. resulted in the marked enhancement of the binding ability of ***histatin*** 8 to the cells. Two bands of ***histatin*** 8 receptor were found by SDS-PAGE (mol. wts. 44 kDa and 41 kDa).

L3 ANSWER 152 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:186089 CAPLUS
DN 118:186089
TI Purification and some properties of a peptide from human parotid saliva which inhibits hemagglutination of Porphyromonas gingivalis
AU Murakami, Yukitaka
CS Fac. Dent., Osaka Univ., Suita, 565, Japan
SO Osaka Daigaku Shigaku Zasshi (1992), 37(1), 47-62 CODEN: ODSZA2; ISSN: 0473-4629
DT Journal
LA Japanese
AB A peptide from human parotid saliva which inhibits hemagglutination of P. gingivalis 381 was purified by ultrafiltration followed by DEAE-Sephadex A-25 column chromatog. and by gel filtration on Sephadex G-25, and then by reverse-phase HPLC. The complete amino acid sequence was as follows; Lys-Phe-His-Glu-Lys-His-His-Ser-His-Arg-Gly-Tyr. The peptide was an active inhibitor of hemagglutination of P. gingivalis 381. The bacterial cells were incubated with the 125I-peptide in the presence or absence of the unlabeled peptide, to evaluate the peptide binding capacity to the cells. The binding of the peptide was rapid, reversible, saturable and specific. The no. of peptide binding sites per cell was 1.5 .times. 104, and the dissocn. const. was in the order of 10-6 M. The binding was increased about 35-fold by addn. of 0.5 mM Cu2+. Crosslinking expt. of 125I-peptide to P. gingivalis cell surface receptor with disuccinimidyl substrate in the addn. of 0.5 mM Cu2+ revealed the presence of two receptors with apparent mol. masses of about 44 and 41 kDa resp.

L3 ANSWER 153 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:122060 CAPLUS
DN 118:122060
TI Binding of synthetic ***histatin*** 8 to oral bacteria
AU Murakami, Yukitaka; Amano, Atsuo; Shizukuishi, Satoshi; Tsunemitsu, Akira
CS Fac. Dent., Osaka Univ., Suita, 565, Japan
SO Koku Eisei Gakkai Zasshi (1992), 42(3), 406-8 CODEN: KEGZA7; ISSN: 0023-2831
DT Journal
LA English
AB ***Histatins*** are histidine-rich polypeptides present in human saliva and salivary glands and have been shown to inhibit the growth of Candida albicans and Streptococcus mutans in vitro. The specific binding activity of 125I- ***histatin*** 8 to oral bacteria was tested. Variable differences in the binding

between 4.degree. and 37.degree. were obsd. in the resp. strain. Porphyromonas, Prevotella, and Capnocytophaga showed comparatively higher binding activity. However, only weak binding to Streptococcus was seen. The specific binding to human red-blood cells was insignificant in comparison to that of P. gingivalis.

L3 ANSWER 154 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:79141 CAPLUS
DN 118:79141
TI Pilot study comparing the salivary cationic protein concentrations in healthy adults and AIDS patients: correlation with antifungal activity
AU Lal, Kamalakshi; Pollock, Jerry J.; Santarpia, R. Peter, III; Heller, Howard M.; Kaufman, H. William; Fuhrer, Jack; Steigbigel, Roy T.
CS Sch. Dent. Med., SUNY, Stony Brook, NY, 11794-8702, USA
SO Journal of Acquired Immune Deficiency Syndromes (1992), 5(9), 904-14 CODEN: JAISET; ISSN: 0894-9255
DT Journal
LA English
AB This investigation compared the salivary cationic protein concns. of 12 healthy adult controls with those of 12 hospitalized patients with AIDS. Salivas were quantified by capillary electrophoresis using purified cationic protein stds. In parotid saliva, histidine-rich polypeptides (HRPs) 1-6, ***histatin*** 6, and lysozyme concns. were detd. In addn. to these eight cationic proteins, submandibular-sublingual saliva was also quantified for ***histatin*** 2 and the ***histatin*** 2 degrdn. product. When comparisons were made on the basis of individual proteins, the HRP- ***histatin*** concns. in the AIDS patients showed either statistically significant decreases or a decreasing trend compared with healthy adult controls. When HRP- ***histatin*** concns. were summed for each patient, there were statistically significant differences between the healthy adult controls and the individuals with AIDS in both parotid and submandibular-sublingual salivas. Closer examn. revealed that some individuals with AIDS had HRP- ***histatin*** concns. that fell within the normal range of the healthy adult controls. For these individuals, lower than expected salivary antifungal values were obtained. Either decreasing histidine-rich protein concns. and/or inability of these proteins in saliva to interact with Candida albicans may contribute to the defective salivary antifungal activity seen in AIDS patients.

L3 ANSWER 155 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:35717 CAPLUS
DN 118:35717
TI Biological role of an arginine residue present in a histidine-rich peptide which inhibits hemagglutination of Porphyromonas gingivalis
AU Murakami, Yukitaka; Tamagawa, Hiroo; Shizukuishi, Satoshi; Tsunemitsu, Akira; Aimoto, Saburo
CS Fac. Dent., Osaka Univ., Suita, 565, Japan
SO FEMS Microbiology Letters (1992), 98(1-3), 201-4 CODEN: FMLED7; ISSN: 0378-1097
DT Journal
LA English
AB The inhibitory effects of synthetic fragments of ***histatin*** 8 (Lys-Phe-His-Glu-Lys-His-His-Ser-His-Arg-Gly-Tyr) on hemagglutination by P. gingivalis 381 were examd. The hemagglutinating activity was reduced much more by the peptide Lys-His-His-Ser-His-Arg-Gly-Tyr than by the peptides Lys-His-His-Ser-His and/or Lys-Phe-His-Glu-Lys. These results suggest that the arginine residue may have an important role in the inhibition of hemagglutination by P. gingivalis.

L3 ANSWER 156 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:4612 CAPLUS
DN 118:4612
TI Adsorption of human salivary proteins to hydroxyapatite: a comparison between whole saliva and glandular salivary secretions
AU Jensen, J. L.; Lamkin, M. S.; Oppenheim, F. G.
CS Sch. Grad. Dent., Boston Univ., Boston, MA, 02118, USA
SO Journal of Dental Research (1992), 71(9), 1569-76 CODEN: JDREAF; ISSN: 0022-0345
DT Journal
LA English
AB The protein compns. of in vitro pellicles formed from whole saliva and parotid and submandibular secretions were detd. by use of synthetic hydroxyapatite as a model for dental enamel. Amylase, acidic and glycosylated proline-rich proteins, statherins, and ***histatins*** were identified in the parotid-derived pellicle. Detailed anal. of the statherin-contg. fractions resulted in the observation of several statherin-like proteins. The use of cationic gel electrophoresis allowed for the identification of ***histatin*** 3 and ***histatin*** 5. The protein compn. of submandibular-derived pellicle was similar to that of parotid-derived pellicle except for the presence of cystatins and the absence of glycosylated proline-rich proteins. In contrast, in vitro pellicle derived from whole saliva exhibited a vastly different compn., consisting primarily of amylase, acidic proline-rich proteins, cystatins, and proteolytically derived peptides. The results indicate that acidic phosphoproteins as well as neutral and basic ***histatins*** from pure secretions selectively adsorb to hydroxyapatite, whereas in whole saliva some of these proteins are proteolytically degraded, dramatically changing its adsorption pattern.

L3 ANSWER 157 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:584848 CAPLUS
DN 117:184848
TI Prophylactic and therapeutic agents containing ***histatins*** for periodontal diseases
IN Kuboki, Yoshinori; Nishikata, Makoto; Kanehira, Takashi; O. Horei; Tazaki, Mariko
PA Sangi Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 3 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- ---------- --------
PI JP 04182420 A2 19920630 JP 1990-311424 19901119
PRAI JP 1990-311424 19901119
AB The title agents contain ***histatin*** 5 (I) or related ***histatin*** derivs. The ***histatins*** specifically inhibit proteinase of periodontal disease-related Bacteroides gingivalis , and are applied in the forms of gargles or dentifrices. The IC50 value of I from human saliva against trypsin-like protease of B. gingivalis was 55 nM.

L3 ANSWER 158 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:404787 CAPLUS
DN 117:4787
TI ***Histatins*** 2 and 4 are autoproteolytic degradation products of human parotid saliva
AU Xu, L.; Lal, K.; Pollock, J. J.
CS Sch. Dent. Med., State Univ. New York, Stony Brook, NY, 11794-8702, USA
SO Oral Microbiology and Immunology (1992), 7(2), 127-8 CODEN: OMIMEE; ISSN: 0902-0055
DT Journal
LA English

AB Freshly collected human parotid saliva contains 8 cationic proteins, as demonstrated by capillary electrophoresis. These proteins include lysozyme, ***histatin*** 6 and the 6 salivary histidine-rich polypeptides (HRPs 1-6). Neither ***histatin*** 2 nor ***histatin*** 4 are present in native undegraded parotid saliva but appear only after autoproteolytic degrdn. of the saliva. ***Histatin*** 2 appears to arise through slow degrdn. of HRP-1, and ***histatin*** 4 is mainly produced as a rapid breakdown product of HRP-3.

L3 ANSWER 159 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:210566 CAPLUS
DN 116:210566
TI The use of capillary electrophoresis to identify cationic proteins in human parotid saliva
AU Lai, K.; Xu, L.; Colburn, J.; Hong, A. L.; Pollock, J. J.
CS Dep. Oral Biol. Pathol., State Univ. New York, Stony Brook, NY, 11794-8702, USA
SO Archives of Oral Biology (1992), 37(1), 7-13 CODEN: AOBIAR; ISSN: 0003-9969
DT Journal
LA English
AB Eight proteins, histidine-rich peptides (HRPs) 1, 2, 3, 4, 5 and 6, lysozyme, and ***histatin*** 6, are the major cationic components of the parotid salivas of normal healthy individuals. ***Histatins*** 2 and 4 appear to be further degrdn. products of the HRPs. Capillary electrophoresis separates all of these eight components, thus allowing future studies to correlate protein concn. with antimicrobial activity in health and disease.

L3 ANSWER 160 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:158619 CAPLUS
DN 116:158619
TI Dentifrices containing peptides
IN Suido, Hirohisa; Katsuta, Tomoko; Nakamura, Shoichi
PA Sunstar, Inc., Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---- ---------- ---- -------- -------------- --------
PI JP 03261717 A2 19911121 JP 1990-59522 19900309 JP 07068111 B4 19950726
PRAI JP 1990-59522 19900309
AB Dentifrices, useful for prevention of dental caries and periodontosis, contain peptides contg. 3-34 amino acid residues and .gtoreq.2 basic amino acids linked together. H-Arg-Lys-Arg-Ala-Arg-Lys-Glu-OH (at 0.1 mM) 97% inhibited adhesion of Bacteroides gingivalis to human gingival epithelial cells. CaCO3 45.0, H-Gly-Tyr-Lys-Arg-Lys-Phe-His-Glu-Lys-His-His-Ser-His-Arg-Gly-Tyr-OH 1.0, Na cellulose 1.0, glycerin 20.0, Na lauryl sulfate 1.5, Na saccharin 0.1, flavor 1.2, and H2O to 100 wt.% were mixed to give a toothpaste.

L3 ANSWER 161 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:602892 CAPLUS
DN 115:202892
TI Binding of a histidine-rich peptide to Porphyromonas gingivalis
AU Murakami, Yukitaka; Shizukuishi, Satoshi; Tsunemitsu, Akira; Nakashima, Kazuhisa; Kato, Yukio; Aimoto, Saburo
CS Fac. Dent., Osaka Univ., Suita, 565, Japan
SO FEMS Microbiology Letters (1991), 82(3), 253-6 CODEN: FMLED7; ISSN: 0378-1097
DT Journal
LA English
AB P. gingivalis 381 cells were incubated with 125I-labeled histidine-rich polypeptide (***histatin***) 5 in the presence or absence of unlabeled ***histatin*** 5, to evaluate the ***histatin*** -binding capacity of the cells. The binding of ***histatin*** 5 was rapid, reversible, saturable and specific. The no. of ***histatin*** 5-binding sites per cell was 3600, and the dissocn. const. (Kd) was in the order of 10-6M. These findings suggest that ***histatin*** interacts with certain bacterial cells through specific binding sites on their surface, and will allow the development of a ***histatin*** radioreceptor assay.

L3 ANSWER 162 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:581315 CAPLUS
DN 115:181315
TI Anticandidial activity of major human salivary ***histatins***
AU Xu, Tao; Levitz, Stuart M.; Diamond, Richard D.; Oppenheim, Frank G.
CS Goldman Sch. Grad. Dent., Boston Univ., Boston, MA, 02118, USA
SO Infection and Immunity (1991), 59(8), 2549-54 CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB Previously it was shown that ***histatins*** 1, 3, and 5 are homologous, histidine-rich proteins present in human parotid and submandibular secretions which contain 38, 32, and 24 amino acids, resp. Interest in these proteins stems from the fact that ***histatins*** exhibit candidacidal and candidastatic activities. The goal of the present investigation was a detailed functional characterization, by using 3 bioassays, of these anticandidal activities of ***histatins*** in killing of blastoconidia, killing of germinated cells, and inhibition of germination. Candidacidal activities were evaluated at several ionic strengths, in the presence of different mono- and divalent ions, and at multiple pH values. The susceptibility of Candida albicans in different growth phases to ***histatins*** was investigated. While all three major human ***histatins*** demonstrated candidacidal activities, they differed in their abilities to kill blastoconidia and germinated cells, with ***histatin*** 5 being the most active, ***histatin*** 3 showing moderate activity, and ***histatin*** 1 exhibiting the lowest level of activity. For the inhibition of germination, however, ***histatin*** 3 exhibited more activity than either ***histatin*** 1 or ***histatin*** 5. The candidacidal activity of ***histatins*** was inversely proportional to both the ionic strength and the divalent cation concn. in the medium. Stepwise redn. of the pH of the assay medium enhanced the candidacidal activities of ***histatins*** 1 and 3, while the activity of ***histatin*** 5 was pH independent over the range of pH 4-8. C. albicans in log-phase growth was more susceptible to ***histatins*** 1 and 3 than cells in stationary phase. Cells in either growth phase were still more vulnerable to ***histatin*** 5 than to ***histatins*** 1 and 3. The results establish the functional relationship of the major ***histatins*** with respect to both their fungicidal and fungistatic activities and provide insights into their activities under ionic and pH conditions likely to be encountered in vivo in the oral cavity. The data point towards possible mechanisms responsible for the anticandidal activities of ***histatins*** .

L3 ANSWER 163 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:581274 CAPLUS
DN 115:181274
TI ***Histatins*** , a family of histidine-rich polypeptides in human saliva. Structural requirements for histamine-releasing activity
AU Ogata, Kenichiro
CS Sch. Dent., Okayama Univ., Okayama, Japan

SO Okayama Shigakkai Zasshi (1991), 10(1), 53-8 CODEN: OSZAE3; ISSN: 0913-3941
DT Journal
LA Japanese
AB The hydrolysis of a major ***histatin*** , ***histatin*** 1, obtained by digestion with V8 protease from Staphylococcus aureus had 5 times higher histamine-releasing activity than the original peptide, and an active fragment peptide with 12 amino acid residues was isolated from it by HPLC. The fragment was 10 times more active than ***histatin*** 1. Amino acid sequencing of this peptide revealed that it corresponds to the sequence of a fragment consisting of the 5th to 16th residues (Lys to Glu) from the N-terminus of ***histatin*** 1, contg. a cluster of basic amino acids. A synthetic peptide with 9 amino acid residues, which corresponds to a fragment of 5th to 13th residue from N-terminal of ***histatin*** 5, also showed comparable activity. Thus, a part of ***histatin*** appears to act on mast cell membrane as a trigger for histamine release.

L3 ANSWER 164 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:579203 CAPLUS
DN 115:179203
TI Inhibitory effects of human salivary ***histatins*** and lysozyme on coaggregation between Porphyromonas gingivalis and Streptococcus mitis
AU Murakami, Yukitaka; Nagata, Hideki; Amano, Atsuo; Takagaki, Masaru; Shizukuishi, Satoshi; Tsunemitsu, Akira; Aimoto, Saburo
CS Fac. Dent., Osaka Univ., Suita, 565, Japan
SO Infection and Immunity (1991), 59(9), 3284-6 CODEN: INFIBR; ISSN: 0019-9567
DT Journal
LA English
AB The effects of ***histatins*** on coaggregation between Porphyromonas gingivalis 381 and Streptococcus mitis ATCC 9811 were investigated by using a turbidimetric assay. The coaggregation activity was significantly inhibited by ***histatins*** 5 and 8 and strongly by lysozyme. Tritium-labeled ***histatin*** 8 bound to P. gingivalis cells but not to S. mitis cells.

L3 ANSWER 165 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:556865 CAPLUS
DN 115:156865
TI ***Histatins*** , a family of histidine-rich polypeptides in human saliva; isolation and histamine-releasing activity
AU Ogata, Kenichiro
CS Dent. Sch., Okayama Univ., Okayama, 700, Japan
SO Shika Kiso Igakkai Zasshi (1990), 32(6), 671-85 CODEN: SHKKAN; ISSN: 0385-0137
DT Journal
LA Japanese
AB Histidine-rich polypeptides with histamine-releasing activity from rat peritoneal mast cells were isolated from human saliva by heparin-Ultrogel affinity chromatog. and reverse-phase high performance liq. chromatog. The amino acid compn. of these peptides showed high proportions of histidine, lysine and arginine. The amino acid sequences detd. by automated Edman degrdn. revealed that these peptides were completely identical to ***histatins*** 1, 3 and 5, resp. ***Histatins*** 3 and 5 induced the histamine release from isolated rat mast cells accompanied with degranulation in a dose-dependent manner over the concn. range 5-40 .mu.M, while ***histatin*** 1 was weakly active. The histamine release by ***histatin*** 5 was completed within 10 s at 37.degree.. The temp. optimum for ***histatin*** 5-induced histamine release was in the range of 25-37.degree., and the release was suppressed at temp. below 15.degree. and above 45.degree.. This activity was obsd. at acid to neutral pH's in the medium, but decreased at alk. pH's. Their actions did not require extracellular calcium. This histamine release was not accompanied by leakage of lactate dehydrogenase. These results indicate that ***histatins*** 1, 3 and 5 can be isolated rapidly from human saliva by using a heparin column and HPLC, and that ***histatin*** 5 induces histamine release by means of calcium-independent exocytosis from the mast cells. It is suggested that ***histatins*** may possibly play a role in an early stage of inflammation in the oral cavity as naturally occurring host-defensive substances.

L3 ANSWER 166 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:490508 CAPLUS
DN 115:90508
TI Primary structure and anticandidal activity of the major ***histatin*** from parotid secretion of the subhuman primate, Macaca fascicularis
AU Xu, T.; Telser, E.; Troxler, R. F.; Oppenheim, F. G.
CS Goldman Sch. Grad. Dent., Boston Univ., Boston, MA, 02118-2392, USA
SO Journal of Dental Research (1990), 69(11), 1717-23 CODEN: JDREAF; ISSN: 0022-0345
DT Journal
LA English
AB A major macaque ***histatin*** (M- ***histatin*** 1) from the parotid secretion of the subhuman primate, M. fascicularis, was isolated by gel filtration on Bio-Gel P-2 and purified to homogeneity by reversed-phase HPLC on a TSK-ODS C18 column. The complete amino acid sequence of M- ***histatin*** 1 was detd. by automated Edman degrdn. M- ***histatin*** 1 contains 38 amino acid residues, a phosphoserine at residue 2, has a mol. wt. of 4881.8, a calcd. pI of 8.5, and histidine forms 26.3% of the mass. The hydropathicity plot of M- ***histatin*** 1 predicts that the mol. is entirely hydrophilic, and Chou-Fasman secondary prediction indicates that the polypeptide is devoid of .alpha.-helix and .beta.-sheet conformation in aq. solns. but contains a series of .beta. turns. M- ***histatin*** 1 includes a 6-amino-acid insert (residue 10-15) not present in human ***histatins*** and, with the introduction of gaps to maximize homol., it displays 89% and 91% sequence similarity with human ***histatins*** 1 and 3, resp. M- ***histatin*** 1 exhibited fungicidal and fungistatic effects against the dimorphic pathogen, Candida albicans, in 3 sep. bioassays. Its anticandidal effects were comparable with, or greater than, those of human ***histatins*** 1, 3, and 5. M- ***histatins*** 2, 3, and 4 were not sequenced directly because insufficient materials were available, bu the amino acid compn. of M- ***histatin*** 3 was nearly identical to that of the N-terminal 20 amino acid residues of M- ***histatin*** 1. There appears to be only one major ***histatin*** in macaque parotid secretion in contrast to the family of ***histatins*** in human parotid and submandibular secretions, and the significance of this in the context of evolution and mechanism of action in anticandidal assays is discussed.

L3 ANSWER 167 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:182598 CAPLUS
DN 114:182598
TI mRNAs for PRPs, statherin, and ***histatins*** in von Ebner's gland tissues
AU Azen, E. A.; Hellekant, G.; Sabatini, L. M.; Warner, T. F.
CS Lab. Genet., Univ. Wisconsin, Madison, WI, 53706, USA
SO Journal of Dental Research (1990), 69(11), 1724-30 CODEN: JDREAF; ISSN: 0022-0345
DT Journal
LA English
AB A search was made for expression of genes for proline-rich proteins (PRPs) and other salivary-type proteins, including

statherin and ***histatins*** , in taste-bud tissues of mice and primates because of previous genetic findings in mice (Azen E. A.; et al., 1986) that Prp and taste genes for certain bitter substances are either the same or closely linked. Taste-bud tissues and other tissues were tested for specific mRNAs with labeled DNA probes by Northern blotting and in situ hybridization. PRP mRNAs were present in von Ebner's glands of mice and macaques, and there was a much greater degree of PRP mRNA induction in mouse parotid (16-fold) than in von Ebner's gland (2-fold) after in vivo isoproterenol stimulation. This difference may be due, in part, to differences in autonomic nerve innervation. Statherin and ***histatin*** mRNAs were found in macaque taste-bud tissues contg. von Ebner's gland, and statherin protein was found in human von Ebner's gland by immunohistochem. The finding of PRP gene expression in von Ebner's gland, whose secretions have been suggested to play a role in taste stimulation, adds further support to a possible function of PRPs in bitter tasting. The possible functions of statherin and ***histatins*** in von Ebner's gland secretions may be related to statherin's regulation of salivary Ca and ***histatins*** ' antibacterial and antifungal properties.

L3 ANSWER 168 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:141344 CAPLUS
DN 114:141344
TI Inhibitory effects of synthetic histidine-rich peptides on hemagglutination by Bacteroides gingivalis 381
AU Murakami, Y.; Takeshita, T.; Shizukuishi, S.; Tsunemitsu, A.; Aimoto, S.
CS Fac. Dent., Osaka Univ., Suita, 565, Japan
SO Archives of Oral Biology (1990), 35(9), 775-7 CODEN: AOBIAR; ISSN: 0003-9969
DT Journal
LA English
AB The hemagglutininating activity of Bacteroides gingivalis 381 was inhibited by the synthetic peptide, Asp-Ser-His-Ala-Lys-Arg-His-His-Gly- Tyr-Lys-Arg-Lys-Phe-His-Glu-Lys-His-His-Ser-His-Arg-Gly-Tyr. However, bradykinin potentiator C, used as control, which does not contain cationic amino acids such as L-histidine, L-arginine and L-lysine, had no inhibitory effect.

L3 ANSWER 169 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:138690 CAPLUS
DN 114:138690
TI Salivary ***histatin*** as an inhibitor of a protease produced by the oral bacterium Bacteroides gingivalis
AU Nishikata, Makoto; Kanehira, Takashi; Oh, Hourei; Tani, Hiroshi; Tazaki, Mariko; Kuboki, Yoshinori
CS Sch. Dent., Hokkaido Univ., Sapporo, 060, Japan
SO Biochemical and Biophysical Research Communications (1991), 174(2), 625-30 CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB The effect of ***histatin*** 5 from human parotid saliva on various proteases was examd. ***Histatin*** 5 strongly inhibited a trypsin-like protease produced by B. gingivalis with an IC50 value of 55 nM. Clostripain was also inhibited (IC50 = 800 nM). Activities of other proteases were not affected significantly. Because B. gingivalis is a suspected periodontal pathogen and its proteolytic enzymes have been considered to be assocd. with periodontal tissue destruction, it is suggested that salivary ***histatins*** play a role as a preventive against periodontal disease.

L3 ANSWER 170 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:60196 CAPLUS
DN 114:60196
TI Purification and characterization from human parotid secretion of a peptide which inhibits hemagglutination of Bacteroides gingivalis 381
AU Murakami, Yukitaka; Amano, Atsuo; Takagaki, Masaru; Shizukuishi, Satoshi; Tsunemitsu, Akira; Aimoto, Saburoo
CS Fac. Dent., Osaka Univ., Osaka, 565, Japan
SO FEMS Microbiology Letters (1990), 72(3), 275-9 CODEN: FMLED7; ISSN: 0378-1097
DT Journal
LA English
AB A peptide from human parotid secretion which inhibited hemagglutination of B. gingivalis 381 was purified by ultrafiltration followed by DEAE-Sephadex A-25 column chromatog. and by gel filtration on Sephadex G-25, and then by reversed-phase HPLC. The complete amino acid sequence of the peptide, detd. by automated Edman degrdn. was as follows: Lys-Phe-His-Glu-Lys-His-His-Ser-His-Arg-Gly-Tyr. The peptide contained 12 residues and the charged amino acids predominated with 4 histidine, 2 lysine, 1 arginine and 1 glutamic acid residues, thus being a histidine-rich peptide. The peptide was an active inhibitor of the hemagglutinating activity of B. gingivalis. Specific binding of tritium-labeled peptide to B. gingivalis cells was demonstrated. The histidine-rich peptide may function as a binding domain for the hemagglutinins of B. gingivalis during agglutination.

L3 ANSWER 171 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:606101 CAPLUS
DN 113:206101
TI Characterization of the genetic origins of ***histatins*** and statherins, secretions of human parotid and submandibular glands
AU VanderSpek, Johanna Catharina
CS Boston Univ., Boston, MA, USA
SO (1990) 236 pp. Avail.: Univ. Microfilms Int., Order No. DA9019706 From: Diss. Abstr. Int. B 1990, 51(2), 593
DT Dissertation
LA English
AB Unavailable

L3 ANSWER 172 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:546119 CAPLUS
DN 113:146119
TI Molecular genetics of human salivary proteins
AU Saitoh, Eiichi; Isemura, Satoko; Sanada, Kazuo
CS Sch. Dent. at Niigata, Nippon Dent. Univ., Niigata, 951, Japan
SO Shigaku (1990), 78(1), 2-20 CODEN: SHIGAZ; ISSN: 0029-8484
DT Journal; General Review
LA Japanese
AB A review with 118 refs. on the genes of proline rich protein (PRP) family of salivary proteins and the mechanism of diversification of PRP by a small no. of alleles, the structure and characterization of cystatin, (cysteine protease inhibitors), and genes of statherin, ***histatin*** , and amylase family.

L3 ANSWER 173 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:513622 CAPLUS
DN 113:113622
TI Rapid purification and characterization of ***histatins*** (histidine-rich polypeptides) from human whole saliva
AU Sugiyama, K.; Ogino, T.; Ogata, K.
CS Dent. Sch., Okayama Univ., Okayama, 700, Japan
SO Archives of Oral Biology (1990), 35(6), 415-19 CODEN: AOBIAR; ISSN: 0003-9969
DT Journal
LA English

AB Three different polypeptides capable of stimulating histamine release from mast cells were isolated from human whole saliva, using heparin-gel chromatog. followed by reversed-phase HPLC. The amino acid sequences of these peptides were shown to be identical to those of ***histatins*** 1, 3 and 5.

L3 ANSWER 174 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:419637 CAPLUS
DN 113:19637
TI Structural relationship between human salivary ***histatins***
AU Troxler, R. F.; Offner, G. D.; Xu, T.; Vanderspek, J. C.; Oppenheim, F. G.
CS Sch. Med., Boston Univ., Boston, MA, 02118, USA
SO Journal of Dental Research (1990), 69(1), 2-6 CODEN: JDREAF; ISSN: 0022-0345
DT Journal
LA English
AB ***Histatins*** are a group of electrophoretically distinct histidine-rich polypeptides with microbicidal activity found in human parotid and submandibular gland secretions. Recently, it was shown that ***histatins*** 1, 3, and 5 are homologous proteins that consist of 38, 32, and 24 amino acid residues, resp., and that these polypeptides kill the pathogenic yeast, Candida albicans. The isolation and structural characterization of ***histatins*** 2, 4, 6, and 7-12, the remaining members of this group of polypeptides, is described here. ***Histatin*** 2 was found to be identical to the C-terminal 26 residues of ***histatin*** 1; ***histatin*** 4 was found to be identical to the C-terminal 20 residues of ***histatin*** 3; and ***histatin*** 6 was found to be identical to ***histatin*** 5, but contained an addnl. C-terminal arginine residue. The amino acid sequences of ***histatins*** 7-12 formally corresponded to residues 12-24, 13-24, 12-25, 13-25, 5-11, and 5-12, resp., of ***histatin*** 3, but could also arise proteolytically from ***histatin*** 5 or 6. These results establish, for the 1st time, the complete structural relations between all members of this group of microbicidal proteins in human parotid saliva. The relation of ***histatins*** to one another is discussed in the context of their genetic origin, biosynthesis, and secretion into the oral cavity, and potential as reagents in anti-candidal studies.

L3 ANSWER 175 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:401356 CAPLUS
DN 113:1356
TI Molecular cloning of human submandibular ***histatins***
AU VanderSpek, J. C.; Offner, G. D.; Troxler, R. F.; Oppenheim, F. G.
CS Sch. Med., Boston Univ., Boston, MA, 02118, USA
SO Archives of Oral Biology (1990), 35(2), 137-43 CODEN: AOBIAR; ISSN: 0003-9969
DT Journal
LA English
AB ***Histatins*** are a group of histidine-rich polypeptides found in human parotid and submandibular gland secretions. These polypeptides are microbiocidal, possibly involved in maintaining the acquired enamel pellicle, and enhance the glycolytic activity of certain oral micro-organisms. ***Histatins*** 1, 3, and 5 are homologous proteins with 38, 32, and 24 amino acid residues, resp.; the cDNAs coding for ***histatins*** 1 and 3 have now been isolated and sequenced. The cDNA sequences were highly homologous but contained differences throughout their length, indicating that they arise from different genes that may be derived from a common ancestral gene. Northern blots were hybridized to a series of oligonucleotide probes, designed on the basis of ***histatin*** cDNA sequences, and these pos. identified mRNAs for ***histatins*** 1 and 3. In addn., there was a third mRNA, which hybridized to several ***histatin*** oligonucleotide probes, suggesting that ***histatin*** 5 might be derived from a distinct mRNA and not by proteolytic processing of ***histatin*** 3. A Northern blot of macaque parotid gland total RNA also showed three ***histatin*** mRNAs, indicating that similar ***histatins*** exist in a non-human primate.

L3 ANSWER 176 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:176781 CAPLUS
DN 112:176781
TI Elevation of salivary antimicrobial proteins following HIV-1 infection
AU Atkinson, Jane C.; Yeh, Chih Ko; Oppenheim, Frank G.; Bermudez, Debra; Baum, Bruce J.; Fox, Philip C.
CS Clin. Invest. Patient Care Branch, Natl. Inst. Dent. Res., Bethesda, MD, 20892, USA
SO Journal of Acquired Immune Deficiency Syndromes (1990), 3(1), 41-8 CODEN: JAISET; ISSN: 0894-9255
DT Journal
LA English
AB Thirty-seven HIV-1-pos. patients contributed salivary samples from individual major salivary glands. Nineteen patients were unmedicated and asymptomatic, and 18 patients had developed signs of AIDS. Salivas from healthy males served as controls. Levels of 4 salivary antimicrobial proteins (lactoferrin, lysozyme, secretory IgA, and ***histatins***) were detd., as well as total fluid output of the major salivary glands. Concns. of all 4 salivary antimicrobial proteins were increased in the stimulated submandibular/sublingual saliva of all HIV-1-pos. patients as well as the subset of unmedicated HIV-1-pos. patients. Those patients with evidence of oral candidiasis had the highest concns. of lysozyme and ***histatins*** , potent antifungal proteins, in their saliva. Although the etiol. of these protein increases is still unknown, these results further document salivary changes following HIV-1 infection.

L3 ANSWER 177 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:153976 CAPLUS
DN 112:153976
TI Salivary ***histatin*** 5: dependence of sequence, chain length, and helical conformation for candidacidal activity
AU Raj, Periathamby Antony; Edgerton, Mira; Levine, Michael J.
CS Sch. Dent. Med., State Univ. New York, Buffalo, NY, 14214, USA
SO Journal of Biological Chemistry (1990), 265(7), 3898-905 CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB ***Histatin*** 5 (Asp1-Ser-His-Ala4-Lys-Arg-His-His8-Gly-Tyr-Lys-Arg12- Lys-Phe-His-Glu16-Lys-His-His-Ser20-His-Arg-Gly-Tyr24), one of the basid histidine-rich peptides present in human parotid saliva and several of its fragments, 1-16 (N16), 9-24 (C16), 11-24 (C14), 13-24 (C12), 15-24 (C10), and 7-16 (M10), were synthesized by solid-phase procedures. Native ***histatin*** 5 from human parotid saliva was also purified. Their antifungal activities on 2 strains of Candida albicans have been studied and their conformational preferences both in aq. and nonaq. solns. examd. by CD. The synthetic ***histatin*** 5, C16, and C14 peptides were highly active and inhibited the growth of C. albicans. The candidacidal activity data of synthetic ***histatin*** 5 were comparable to the values of the native ***histatin*** 5 isolated from parotid saliva and those reported previously, although the assay system used and the strains examd. were different. The C16 fragment was as active as the whole peptide itself, whereas the N16 fragment was far less active than C148, suggesting that the sequence at the C-terminal

is important for its fungicidal activity. An increase in the chain length of the C-terminal sequence from 12 to 16 residues increased the candidacidal activity, thereby indicating that a peptide chain length of .gtoreq.12 residues is necessary to elicit optimum biol. activity. The CD spectra of these linear peptides showed that they are structurally more flexible, and they adopt different conformations depending on the solvent environment. CD studies provided evidence that ***histatin*** 5 and the longer fragments, C16, N16, and C14 preferred .alpha.-helical conformations in nonaq. solvents such as trifluoroethanol and methanol, whereas in water and pH 7.4 phosphate buffers, they favored random coil structures. The shorter sequences seemed to adopt either turn structures or unordered structures both in aq. and non-aq. solns. It appears that the sequence at the C-terminal of ***histatin*** 5 with a min. chain length of 14 residues and .alpha.-helical conformation are the important structural requirements for appreciable candidacidal activity.

L3 ANSWER 178 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:31418 CAPLUS
DN 112:31418
TI ***Histatins*** , a family of salivary histidine-rich proteins, are encoded by at least two loci (HIS1 and HIS2)
AU Sabatini, L. M.; Azen, E. A.
CS Dep. Med. Genet., Univ. Wisconsin, Madison, WI, 53706, USA
SO Biochemical and Biophysical Research Communications (1989), 160(2), 495-502 CODEN: BBRCA9; ISSN: 0006-291X
DT Journal
LA English
AB A human parotid gland cDNA library was screened with mixed synthetic oligonucleotide probes representing a central coding region common to ***histatins*** 1 and 3. Sequence anal. of 12 ***histatin*** cDNA clones strongly suggests that the ***histatin*** protein family is encoded by at least two closely related loci (HIS1 and HIS2) such that ***histatins*** 1 and 3 are primary products of HIS11 and HIS21 alleles, resp., and that ***histatins*** 4-6 are derived from ***histatin*** 3 by proteolysis. Addnl. data are presented indicating that ***histatin*** 2 may represent the non-phosphorylated form of ***histatin*** 1.

L3 ANSWER 179 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:626301 CAPLUS
DN 111:226301
TI Localization of the genes for ***histatins*** to human chromosome 4q13 and tissue distribution of the mRNAs
AU VanderSpek, Johanna C.; Wyandt, Herman E.; Skare, James C.; Milunsky, Aubrey; Oppenheim, Frank G.; Troxler, Robert F.
CS Sch. Med., Boston Univ., Boston, MA, 02118, USA
SO American Journal of Human Genetics (1989), 45(3), 381-7 CODEN: AJHGAG; ISSN: 0002-9297
DT Journal
LA English
AB A cDNA coding for ***histatin*** 1 was isolated from a human submandibular-gland library and sequenced. This cDNA was used to probe RNAs isolated from a variety of tissues to investigate tissue-specific regulation and to det. whether ***histatins*** might play a role other than in the oral cavity. The same probe was also used for Southern blot anal. of human genomic DNA restricted with various enzymes, and it showed that the genes coding for ***histatins*** are on the same chromosome. In situ hybridization of the cDNA probe to metaphase chromosome spreads was performed to det. chromosomal location of the genes for ***histatins*** . A genomic fragment isolated using the cDNA probe was also hybridized to chromosome spreads, and the same chromosome was identified. The genes for ***histatins*** are located on chromosome 4, band q13. Three ***histatin*** mRNAs are expressed in human parotid and submandibular glands but in none of the other tissues studied. These results suggest that ***histatins*** are specific to salivary secretions.

L3 ANSWER 180 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:531285 CAPLUS
DN 111:131285
TI Tissue distribution of RNAs for cystatins, ***histatins*** , statherin, and proline-rich salivary proteins in humans and macaques
AU Sabatini, L. M.; Warner, T. F.; Saitoh, E.; Azen, E. A.
CS Dep. Med. Genet., Univ. Wisconsin, Madison, WI, 53706, USA
SO Journal of Dental Research (1989), 68(7), 1138-45 CODEN: JDREAF; ISSN: 0022-0345
DT Journal
LA English
AB The tissue distribution of the mRNAs for a no. of salivary proteins [proline-rich proteins (PRPs), statherin, cystatins, and the ***histatins***] was examd. in humans and macaques to investigate their possible functions and tissue-specific regulation. PRP RNAs (0.8-1.5 kb) are expressed in human and rhesus parotid and submandibular glands, and in the human bronchus. The genes for the acidic and basic PRPs are differentially regulated in these tissues. RNAs for acidic PRPs are predominantly expressed in the submandibular gland, for basic PRPs in the respiratory tract, and for both acidic and basic PRPs in the parotid gland. Protein studies of secretions from these tissues confirm the RNA results. Statherin RNA (0.65 kb) was detected in human and rhesus parotid and submandibular glands and the human bronchus, as well as in rhesus lacrimal glands. Statherin was found by tissue immunoperoxidase staining in the serous cells of respiratory tract submucosal glands, which is the same location for the synthesis of PRPs. Several cystatin RNAs (0.8-1.3 kb) were differentially expressed in human parotid glands, submandibular glands, and the bronchus, and in lacrimal glands from both rhesus and cynomolgus macaques. RNAs (0.6 kb) for the ***histatins*** were found only in parotid and submandibular glands. Thus, it appears that PRPs, statherin, and cystatins may play a broader role in the physiol. of biol. fluids and secretions than previously suspected, since they are found in secretions other than saliva. However, the functions of the ***histatins*** are restricted to saliva. These studies also pose some interesting questions regarding the differential expression of these genes in a variety of secretory tissues.

L3 ANSWER 181 OF 181 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:506684 CAPLUS
DN 109:106684
TI ***Histatins*** , a novel family of histidine-rich proteins in human parotid secretion. Isolation, characterization, primary structure, and fungistatic effects on Candida albicans
AU Oppenheim, Frank G.; Xu, Tao; McMillian, Frederica M.; Levitz, Stuart M.; Diamond, Richard D.; Offner, Gwynneth D.; Troxler, Robert F.
CS Goldman Sch. Grad. Dent., Boston Univ., Boston, MA, 02118, USA
SO Journal of Biological Chemistry (1988), 263(16), 7472-7 CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB ***Histatins*** 1, 3, and 5 from human parotid secretion were isolated by gel filtration on Bio-Gel P-2 and reverse-phase HPLC. The complete amino acid sequences of ***histatins*** were detd. by automated Edman degrdn. of the proteins, Staphylococcus aureus V8 protease, and tryptic peptides. ***Histatins*** 1, 3, and 5 contained 38, 32, and 24 amino acid

residues, had mol. wts. of 4929, 4063, and 3037, resp., and contained 7 residues of histidine. ***Histatin*** 1 contained 1 mol phosphate/mol protein; ***histatins*** 3 and 5 lacked phosphate. With the exception of glutamate (residue 4) and arginine (residue 11) in ***histatin*** 1, the 1st 22 amino acid residues of all 3 ***histatins*** were identical, and the C-terminal 7 residues of ***histatins*** 1 and 3 were also identical. The sequence, Glu-Phe-Pro-Phe-Tyr-Gly-Asp-Tyr-Gly (residues 23-29), in ***histatin*** 1 was absent in ***histatin*** 3; and the sequence, Gly-Tyr-Arg (residues 23-25), in ***histatin*** 3 was absent in ***histatin*** 1. The complete sequence of ***histatin*** 5 was contained within the N-terminal 24 residues of ***histatin*** 3. The structural data suggested that ***histatins*** 1 and 3 are derived from different structural genes, whereas ***histatin*** 5 is a proteolytic product of ***histatin*** 3. All 3 ***histatins*** exhibited the ability to kill the pathogenic yeast, Candida albicans.

=> log y
COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION
FULL ESTIMATED COST 465.81 466.02

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION
CA SUBSCRIBER PRICE -123.35 -123.35

STN INTERNATIONAL LOGOFF AT 12:27:36 ON 20 JAN 2004